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CONTENTS.

PAGE

Transfusion of Blood. History, Methods, Dangers, Preliminary Tests, Present Status. Report of One Hundred and Fifty Transfusions.
By Roy D. McClure, M. D., F. A. C. S., and George Robert Dunn, M. D. 99

Aleucocythæmic Leukæmia. 1. Acute Myeloblastic Leukæmia. 2. Chloroma (?). 3. Chronic Lymphatic Leukæmia. (Illustrated).
By John T. King, Jr., M. D. 114

Observations Bearing on the Possibility of Developing an Experimental Chemotherapy of Tuberculosis.
By Paul A. Lewis, M. D. 120

Notes on New Books 125

TRANSFUSION OF BLOOD.

HISTORY, METHODS, DANGERS, PRELIMINARY TESTS, PRESENT STATUS. REPORT OF ONE HUNDRED AND FIFTY TRANSFUSIONS.

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From the very earliest times, the blood has been regarded as synonymous with life. It was considered by the ancients as the seat of the soul. In the Bible[1] we have the following: "Because the life of the flesh is in the blood and I have given it to you upon the altar to make an atonement for your souls: for it is the blood that maketh an atonement for the soul." Many references are made to transfusion of blood in the writings of the ancient Egyptians. It was condemned by Pliny and Celsus. In the Metamorphoses of Ovid[2] we have: "Quid nunc dubitatis inertes? Stringite, ait, gladios; veteremque haurite cruorem, ut repleam vacuas juvenili sanguine venas." "Why, now, do ye hesitate and do nothing? Unsheathe your swords and draw out the old blood, that I may fill the empty veins with the blood of the youth." Libavius in 1615 reports in "Defensione Syntagmatis arcanorum chymicorum" as follows: "Let there be present a robust, healthy youth full of lively blood. Let there come one exhausted in strength, weak, enervated, scarcely breathing. Let the master of the art [the operator] have silver tubes that can be adapted one to the other; then let him open an artery of the healthy one, insert the tube and secure it. Next let him incise the artery of the patient and put into it the feminine [receiving] tube. Now let him adapt the two tubes to each other and the arterial blood of the healthy one, warm and full of spirit, will leap into the [vessels of the] sick one, and immediately will bring to him the fountain of life and will drive away all languor."

It is recorded that Jean Baptiste Denys[3] of Montpellier, physician to Louis XIV, performed the first transfusion of blood in man. In June, 1667, he injected the blood of a calf or a lamb into the veins of a young man dying from repeated venesections. The patient survived and apparently recovered his health. Violent controversies arose regarding the operation, and it was decreed that for the future no transfusion should be made on the human body except with the approbation of the physicians of the Faculty of Paris.

One hundred and seventy-five years earlier than this, however, there is a report of the transfusion of Pope Innocent VIII. The following is copied from Villari's Life of Savonarola:[4] "The vital powers of Innocent VIII rapidly gave way. He had for some time fallen into a kind of somnolency, which was sometimes so profound that the whole court be-

lieved him to be dead. All means to awaken the exhausted vitality had been resorted to in vain, when a Jew doctor proposed to do so by the transfusion, by means of a new instrument, of the blood of a young person; an experiment which hitherto had been made only on animals. Accordingly, the blood of the decrepit old Pontiff was passed into the veins of a youth, whose blood was transferred into those of the old man. The experiment was tried three times, and at the cost of the lives of three boys, probably from air getting into their veins, but without any effect to save that of the Pope. He expired on the 25th of April, 1492." However, another version, contradicting the above is found in "The Life and Times of Rodrigo Borgia:"[5] "Three boys were bled until they died, and the Pope drank a draught prepared from this blood, without benefit." It seems probable that transfusions of blood were attempted before the time of Harvey's discovery of the circulation of the blood in the 17th century.

In the diary of Samuel Pepys we read:

"November 14, 1666, Dr. Croone told me, that, at the meeting at Gresham College tonight, which, it seems, they now have every Wednesday again, there was a pretty experiment of the blood on one dogg let out till he died into the body of another on one side, while all his own ran out on the other side. The first died upon the place. The other very well, and likely to do very well. This did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like; but, as Dr. Croone says, may, if it takes, be of mighty use to man's health, for the amending of bad blood by borrowing from a better body."

In a footnote the following:

"At the meeting on November 14th, the experiment of transfusing blood of one dog into another was made before the Society by Mr. King and Mr. Thomas Coxe upon a little mastiff and a spaniel with very good success, the former bleeding to death, and the latter receiving the blood of the other, and emitting so much of his own as to make him capable of receiving that of the other."

On November 21[6] the spaniel "was produced and found very well." The experiment of transfusions of blood which occupied much of the attention of the Royal Society in its early days has been revived within the last few years.

"November 16. This noon I met with Mr. Hooke, and he tells me the dog which was filled with another dog's blood, at the College the other day, is very well, and like to be so as ever, and doubts not its being found of great use to men; and so to Dr. Whistler, who dined with us at the tavern."

Denys reports several transfusions, from 5 to 10 ounces of arterial blood of a lamb being usually employed; the first, the depletion from the venesection case, with complete cure; the second purely experimental, a perfectly healthy man agreeing to the trial. Ten ounces of blood were removed from his vein and a similar amount from a lamb was injected into him. No disagreeable results were noted, and the man experienced an agreeable sensation of warmth. The third case was in a man, 34 years old, who had escaped from a place of confinement, having been insane for eight years. He was captured and transfused by Denys with five or six ounces of blood from a calf. As soon as he became calm a larger quantity was used. The disapprobation of the Faculty of Paris discouraged further transfusions in France until early in the 19th century.

About the time that Denys was working in France, Lower[7] was carrying on similar experiments in England. He reports his discoveries beginning with the year 1683, though before this, as far back as 1666, he had transfused the blood of three calves into three dogs. One of the dogs "from which so much blood had been drawn the day before that he could hardly stir any more, having been supplied the next morning with the blood of a calf, recovered instantly his strength and showed a surprising vigor."

This is the method of transfusion described by Dr. Lower:

"First take up the Carotidal Artery of the Dog or other Animal, whose blood is to be transfused into another of the same or different Kind, and separate it from the Nerve of the 8th Pair, and lay it bare above an Inch. Then make a strong ligature on the upper Part of the Artery not to be untied again: But an Inch below, viz. towards the Heart, make another Ligature of a running Knot, which may be loosened or fastened as there shall be Occasion. Having made these two Knots, draw two Threads under the Artery between the two Ligatures: and then open the artery, and put in a quill, and tie the Artery upon the Quill very fast by those two Threads, and stop the Quill with a Stick. After this, make bare the Jugular Vein, in the other Dog, about an Inch and a Half long: and at each End make a Ligature with a running Knot, and in the Space between the two running Knots draw under the Vein two Threads as in the other: Then make an Incision in the Vein, and put into it two Quills, one into the descendent Part of the Vein, to receive the Blood from the other Dog, and carry it to the Heart: and the other Quill put into the other Part of the Jugular Vein (Which comes from the Head) out of which the second Dog's own Blood must run in the Dishes. These two Quills being put in and tied fast, stop them with a Stick, till there be occasion to open them. All Things being thus prepared, fasten the Dogs on their Sides towards one another so conveniently that the Quills may go into each other. After that unstop the Quill that goes down into the first Dog's Jugular Vein, and the other Quill coming out of the other Dog's Artery; and by the help of two or three other Quills, put into each other, according as there shall be occasion, insert them into one another. Then slip the running Knots, and immediately the Blood runs through the Quills, as through an Artery, very impetuously. And immediately, as the Blood runs into the Dog, unstop the other Quills, coming out of the upper Part of his Jugular Vein (a Ligature being first made about his Neck, or else his other Jugular Vein being compressed by one's Finger) and let his own blood run out at the same Time into Dishes (not constantly, but according as you perceive him able to bear it) till the other Dog begins to cry, and faint, and fall into Convulsions, and at last die by his Side.

"Then take out both Quills out of the Dog's Jugular Vein, and tie the running Knot fast, and cut the Vein asunder (which you may do without any Harm to the Dog, one Jugular Vein being sufficient to convey all the Blood from the Head and upper Parts, by reason of a large Anastomosis, whereby both the Jugular Veins meet the Larynx.) This done, sew up the Skin, and dismiss him, and the Dog will leap from the Table, and shake himself, and run away as if nothing ailed him.

"Or, instead of a Quill, take a small crooked Pipe of Silver or Brass, so slender that one End may enter into a Quill; and having at the other End, that is to enter into the Vein and Artery, a small Knob, and for the better fastening them to it with a Thread; for this is much more easy to be managed than a Quill."

There is much interesting material in this article by Dr. Lower. For instance, he reports the cure of a mangy dog in ten days after transfusions with blood from a healthy dog.

He reports the transfusion of a dog for acute anemia following splenectomy with hemorrhage. He cites a letter from M. Denys from Paris concerning the transfusion of a 26-year-old horse with the blood of four wethers. Many transfusions were done from one species to another.

He reports in detail the experiment of transfusing the blood into human veins by Dr. Arthur Coga, November 23, 1667. The patient was bled seven ounces and then joined to the artery of a sheep by means of the Lower "pipe." The transfusion continued two minutes. It was estimated that 9 or 10 ounces were received into the man's veins. "The man, after the operation as well as in it, found himself very well."

He also reports experiments with non-coagulates, such as spirits of sal ammoniac. Dr. Lower died in 1691. His experiments were repeated by Sir Edmund King, Thomas Coxe, Gayant and Denys.

Then followed a long interval during which transfusion appears to have fallen into disrepute. During the Franco-Prussian War and afterward transfusion was in vogue, but was again given up. Between 1850 and 1875 many transfusion experiments were being carried on in the physiological laboratory of Greifswald. Leisrink was also working with transfusion in Hamburg. The work in Greifswald was being done by Eulenburg and Landois. The latter devised an apparatus for the direct transfusion of blood from the vein of the donor to the vein of the recipient by means of cannulas and tubing. In 1875 he published his monograph, "Die Transfusion des Blutes."

In this country the first article which we found was by Dr. William S. Halsted.[7] He reports several cases of carbon-monoxide poisoning treated by transfusion or refusion of blood. He first drew the blood, defibrinated it, and then reinjected it into the patient. "Refusion of blood is literally a depletory transfusion in which the blood withdrawn is returned to the circulation of the loser."

As to the best methods of infusing fluids into the circulation good authorities disagree. Of the four possible methods, centrifugally or centripetally into an artery or vein, the question of centrifugal venous infusion is mentioned only to be discarded. Hueter, who gives to von Graefe the honor of being the first to draw attention to centrifugal arterial transfusion, deserves the credit of having introduced it to the profession and strongly advocated the method. Kümmell, Schede's assistant, produced gangrene of the hand by the centrifugal infusion of a saline solution into the radial artery. Hueter's arguments for peripheral or centrifugal arterial transfusion are, that the blood courses more slowly and more uniformly to the heart and the danger of phlebitis is avoided. Landois adds to these advantages another—that the capillary system, like a supplementary filter, catches all foreign articles which may be present. Dr. Halsted advocated the centripetal arterial infusion, since the above arguments hold good for centripetal as well as centrifugal arterial transfusion.

The syringe method of transfusion which we have been using for the past year was perfected by Lindeman.[8] The first report made on it was in 1892 by Prof. von Ziemssen.[9] Von Ziemssen at first injected whole blood subcutaneously, and used vigorous massage for 15 minutes. The procedure was very painful, since he used 300 to 450 cc. of blood at an injection. The hemoglobin was increased by 10 to 15 per cent and von Ziemssen reports that there was no fever and no hemoglobinuria in these cases. Next he devised the method of syringes. He inserted a needle into the vein, withdrew a syringe full of blood and injected it through a needle already inserted into the vein of the recipient. He advised at least three syringes of a capacity of 25 cc., so that while one was being filled and one being emptied, the other one could be cleaned out with sterile salt solution. Following the intravenous infusion he occasionally noted a rise of temperature and chill, but in no case was there hemoglobinuria. There was no evidence of hemolysis, and no free hemoglobin was found in the blood serum. He encountered no phlebitis or secondary thrombosis and he found that the needle could be stuck into the vein again at the same place. He always had a number of needles ready. His average transfusion was from 200 to 300 cc. Von Ziemssen first raised the question whether often repeated transfusions in the bad progressive anemias might have a use, and suggested the possibility that by these means a real cure might result in some of these cases. He reports one case of anemia in a woman, 38 years old, whom he transfused seven times with marked benefit each time and a rise in the hemoglobin. He experimented on the relative value of blood transfusions and saline infusions and concluded that the salt infusion was of benefit only for a short time.

The next great steps were made in this country chiefly in the line of simplifying the technique and making more sure of success in transferring a sufficient quantity of blood from the donor to the recipient. The work of Carrel[10] on the direct successful end-to-end suture of blood vessels (as well as the cannula devised by Crile),[11] added a new interest. Before this time, excepting for the work of von Ziemssen, one could not be certain that any blood would enter the veins of the recipient. During the past few years multitudes of cannulas and methods of suture have been devised. These newer methods have made safe the transfer of blood without the former danger of clotting and subsequent embolism.

BRIEF REPORT OF SUTURES AND CANNULAS.

Carrel's success, as you know, was due mainly to the most rigid aseptic technique and the prevention of blood clotting in the wound, or in the severed blood vessels during the operation, by means of careful hemostasis and saline irrigation. His manual dexterity, fine needles and suture materials and exact approximation of intima and media, were also important factors. Then came the Crile cannula with the principle of everting one vessel over a hollow cylinder and inserting this into the recipient vessel. In this method the intima coats are brought together and there are no raw surfaces. Follow-

ing this there came a number of imitations with improvements, the best of these being the Elsberg[12] cannula. Sauerbruch[13] and Hartwell[14] devised a method of slipping the ends of the artery directly into the end of the vein. This was fairly successful. Levin,[15] Janeway,[16] Soresi[17] and McGrath[18] employed methods more or less similar, the vessels being everted over hollow cylinders and then brought together directly end-on, by sliding the two parts on a little track or by closing a clamp.

The main objection to all of these methods is that they cause a considerable amount of inconvenience to both donor and recipient. The amount of blood cannot be determined absolutely excepting, perhaps, by methods suggested by Libman and Ottenberg.[19] Oftentimes the artery would go into a spasm from which it would not recover for half an hour or more, so that only a very small quantity of blood could pass through. This spasm sometimes could be overcome by irrigagations of hot salt solution.

Then came the indirect methods, that is, methods in which the blood, while being transferred, comes in contact with the walls of the cannula, a receptacle, a needle or a syringe. The first of these was carried out in London in 1666 by Dr. Lower; the first from man to man in France by Denys, who used quills described above. Landois,[20] about 1860, used the rubber tubes. These methods were probably unsatisfactory. In 1909 Brewer and Leggett[21] used simple glass tubes coated with paraffin extending from the vessel of the donor to the vessel of the recipient. This proved to be a very efficient method. Pope[22] modified it somewhat by using a rubber tube between two glass cannulas. Bernheim[23] used the silver cannula, one-half being fitted into the artery of the donor, the other into the vein of the recipient—one cannula then fits into the other, completing the connection.

Blood Withdrawn and Reinjected.

For the prevention of clotting most of these methods, for instance, those of Curtis and David[24] (1911), depend upon paraffin-coated receptacles. Kimpton and Brown,[25] Satterlee and Hooper,[26] and Percy,[27] developed methods for measuring the blood and then reinjecting it. In none of these was there at first an addition of any foreign element. The best of these methods is apparently that devised by Kimpton and Brown: the blood can be withdrawn in one room and taken into another for injection into the recipient.

The greatest advance that has been made in solving the technical difficulties of transfusion came with the introduction of the syringe method. It is so easy and so simple, causing no inconvenience to either donor or recipient, that it is almost an ideal method. Whether ultimately only one syringe or several will be used is yet to be determined. The syringe method[28]* was first described and used by Prof. H. von Ziemssen, Director of the Medical Clinic in Munich, in 1892.[9] He used a number of needles which were put directly into the veins of recipient and donor. He advised at least three syringes of 25 cc. and two or three assistants. The syringe was filled with blood from the donor, which was then injected directly into the recipient. While this injection was being made, the second syringe was being filled. When the first syringe was emptied of its blood it was immediately washed out with normal salt solution by an assistant, so that a continuous transfusion was going on. He reports a number of cases treated by this method, the average transfusion being about 300 cc.

On April 10, 1913, before the New York Academy of Medicine, Lindeman reported an elaboration of this method by the use of improved needles and more syringes. Von Ziemssen's method had been practically forgotten and Lindeman's revival was apparently a great advance.

Recently there have been invented several devices by means of which only one syringe is used, as in that of Watts (not reported) in Dr. Halsted's Clinic, and in those of Kush,[29] Bernheim,[30] Cooley and Vaughan,[31] and then later of Unger[32] in New York. The Unger apparatus is probably the best. A continuous injection of salt solution is made through the apparatus so that the blood does not have time to clot in it. The syringe is kept cool by means of an ether spray which retards clotting. There is but little danger of any infection being carried from recipient to donor.

Herudin and Sodium Citrate, Plasmaphæresis Methods.

At the same time that work was being done to find a mechanical way of preventing clotting, that is, a more rapid or more perfect way of transferring the blood, investigators were turning their attention to the chemical side of the problem with the hope that if the blood could be kept from clotting by means of some chemical, the difficulty of transfusion would be immediately solved. The two chemicals most used have been herudin and sodium citrate. Prof. John Abel[33] has done a great amount of work along the line which has led up to his plasmaphæresis method, and we have tried this in one patient with uremia in this hospital.

Blood was withdrawn from the patient into receptacles containing herudin. These receptacles were taken for some distance to the laboratory. The red corpuscles were separated from the plasma, then brought back to the operating room and reinjected into the patient in normal salt solution.

Satterlee and Hooper in New York during 1914 reported favorably on the herudin method. The sodium citrate method was reported by three workers almost simultaneously; first, however, by Hustin,[34] from Brussels, a little later in this country by Weil[35] and then by Lewisohn[36]—each publishing his article early in 1915. These methods have proved very successful and have the advantage that blood may be kept for some time, even four or five days, on ice and then be injected into the recipient.

At first the objection was made that the use of any drug to delay coagulation time would contra-indicate the transfusion, since in a great many cases in which transfusion is indicated there is already bleeding with increased coagulation

* Blundell (1818) was probably the first man to use the syringe in transfusion, although since he employed only one syringe, he could not transfer very large quantities of blood.

time. With oxalate and citrate solutions the calcium of the blood is fixed, and the calcium is a necessary factor in spontaneous coagulation. Practice with the method, however, apparently has shown that the coagulation time of the recipient is not lengthened but is actually shortened. This is hard to explain.

Defibrinated Blood.—The syringe method and the citrate method of transfusion appear to us to have forever abolished any justification for the injection of defibrinated blood, although this procedure has saved lives and done a great deal of good. The reaction, however, with chill and high fever after the injection of defibrinated blood in so many cases would indicate that the method should be given up.

The work of Dr. Halsted in 1882, and that of Dr. Moss[37] with defibrinated blood should not be forgotten. Dr. Halsted concluded from his work with the cases of gas poisoning that the depletion and not the refusion was the more beneficial.

Hemolysis.—If the mechanical difficulties had been the only ones to be overcome, we are sure that transfusion would now have a far different standing in the medical world. Discredit must have repeatedly been thrown on the procedure by the accidents, often fatal, due to hemolysis. It was Landois who first showed that the serum of one animal may have the property of destroying the red blood cells in another. Hayem[38] reported that in a transfusion from an ox to a dog, a serious condition resulted, resembling purpura hemorrhagica, death occurring in a few hours. He says: "The effect of a foreign cell on the circulating blood is such that the latter immediately becomes finely clotted and carries the thousands of clots into the small vessels, and one sees innumerable infarcts formed." In the present paper we shall not discuss the development of knowledge along these lines and the serological tests which have become so essential.

Eight or nine years ago, great discredit was thrown upon these laboratory tests by most of the men doing transfusion. It was the common saying that hemolysis or agglutination might occur *in vitro* but not *in vivo* and vice versa. At first I agreed with this attitude and, while in New York,[39] good fortune was on my side and I had no serious accidents. Later, however, I became convinced of the great importance of these tests and shall never again consent to do a transfusion except under the most extreme urgency without the proper report from these laboratory tests. The fault, at first, probably was due to the fact that the tests were not allowed to run long enough. We firmly believe now that they should be negative at the end of one hour—never less—or, if possible, after a longer observation. All diseases transmissible by transfusion must be carefully ruled out by careful and accurate examinations.

Transfusion has been tried in the following conditions: pernicious anemia, illuminating-gas poisoning, exophthalmic goitre, hemophilia, toxemia, shock, hemorrhage, leukemia, septicemia, purpura hemorrhagica, malnutrition, endocarditis, intoxication, general debility, dysentery, typhoid fever, infectious diseases, melena neonatorum, scarlet fever, pellagra, tuberculosis and tumors. It has also been used for vaccinating purposes.

The best results have been obtained in hemophiliacs and babies with melena neonatorum; in the latter it is a specific, and in the former it stops the bleeding immediately, although without curing the disease. It is of great benefit in all anemias and with proper regulation may be of still more benefit in the primary types. Thus far, in shock it has been disappointing. This may very well be due to the fact that the shock has progressed too far before the transfusion has been done. We would advise a very early transfusion in cases of shock.

Following acute and prolonged hemorrhages transfusion is of the greatest benefit. For gas poisoning, bleeding is beneficial, as was pointed out by Halsted. Depletion followed by injections of saline solution is as good, if not better, than transfusion. In tuberculosis there has been only slight benefit and, so far, nothing has been accomplished by transfusion in malignant diseases in man.

Vaccinating Transfusion.—There is a great field still to be developed along these lines. Our experiences in typhoid fever have been very satisfactory. It would be very desirable to have a series of donors who have recently had typhoid fever ready to give blood to very ill typhoid patients. In one patient, depleted by hemorrhages as well as having a high-grade toxemia, the transfusion of blood, from a person who had previously had typhoid fever, brought about the most marked improvement, the temperature dropping to normal and the hemorrhage ceasing, with a temporary disappearance of the toxemia. This is very suggestive of the good that might be accomplished by transfusing typhoid fever patients with blood from patients who have recently had the disease and who have probably a high grade of immunity. It would be interesting to try this type of transfusion in patients with other diseases and the procedure might prove very beneficial.

REPORT OF OUR TRANSFUSIONS.

We have done 150 transfusions for 80 patients, as shown in the following table:

Groups of Cases.	Cases.	Transfusions.
1. Pernicious Anemia *	17	64
2. Secondary Anemia	19	23
3. Hemophilia	2	5
4. Shock	2	2
5. Hemorrhage	6	6
6. Leukemia	5	6
7. Intoxications	7	9
8. Septicemia	3	11
9. Dysentery	1	1
10. Typhoid Fever	4	6
11. Other Infections	5	5
12. Purpura Hemorrhagica	1	1
13. Benzol Poisoning	3	8
14. Tumors (Carcinoma)	5	5
	80	152
Not successful (early days, direct method)	2	2
	78	150

* McClure, Roy D.: Pernicious Anemia Treated by Splenectomy and Systematic Often-Repeated Transfusion of Blood. Transfusion in Benzol Poisoning. J. Am. M. Ass., Sept. 9, 1916.

The reactions from the transfusions are shown in the following table. One death was surely due to the transfusion as an immediate cause, owing to the improper matching of the blood.

SUMMARY.

Reaction.	In Transfusions.	Per Cent.
Severe Reaction	20	13⅓
Slight Reaction	25	16⅔
Chill	15	10
Dilated Heart	2	1⅓
Jaundice	1	⅔
Hemoglobinuria	4	2⅔
Temp. Elevation of over 101° F.	34	22⅔
Skin Eruptions	8	5⅓
Agglutination	6	4
Hemolysis	8	5⅓
Results.		
Life Saving	15	10
Beneficial	63	42
No benefit	56	37⅓
Harmful	16	10⅔
		100.0
Not successful. Omitted from calculations (early days, direct method)	2	
	152	

(Two deaths probably due to transfusion, or 1⅓%; certainly one death.)

ing 5 cc. of salt solution, and immediately shaken to distribute the cells. If the patient's blood count is low, more drops are taken—*i. e.*, if the count is 1,000,000, take five drops instead of one.

N. B.—Specimens 1 and 2 are obtained from the patient and from each prospective donor.

3. *Carrying Out the Test.*—(a) As soon as set up, the preparations should be examined to see that the suspension is uniform. The proper thickness is about that of a well-spread blood film—the cells should be close together but not clumped.

(b) Examine at the end of ten minutes. If clumping has occurred in either preparation, the bloods belong to different groups and are incompatible. If no clumping has occurred, then:

(c) Incubate at 37° C. for *one hour.*

(d) Read tests. If clumping has occurred, the bloods belong to different groups and are incompatible. If no clumping in either preparation—the bloods belong to the same group and are compatible.

In the patients for whom many transfusions have had to be done it has been observed that it is more and more difficult to find donors whose blood will match that of the patient. A donor may match perfectly early in the series of transfusions and later be found to be unsuitable. This is probably due to

	Number of Cases.	Number of Transfusions.	Severe Reactions.	Slight Reactions.	Chill.	Dilated Heart.	Jaundice.	Hemoglobinuria.	Temperature Elevation over 101°.	Skin Eruption.	Agglutination.	Hemolysis.	Life Saving.	Beneficial.	No Benefit.	Harmful.	Unsuccessful.	Death.
Pernicious anemia	17	64	7–10%	12–19% †	7–10%	1 (24 hrs. after trans.) 1½% †	1–1½% †	3–4½% †	12–19% †	7–10%	0	0	0	34–53%	23–35%	7–10%	0	0
Secondary anemia	19	23	5	3	2	0	0	1	8	0	2*	2*	2	10	5	4	2	1
Hemophilia	2	5	0	0	0	0	0	0	0	0	0	0	4	0	1	0	0	0
Shock	2	2	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
Hemorrhage	6	6	1	0	1	0	0	0	1	0	1(?)	1(?)	0	2	3	1	0	0
Leukemia	5	6	2	0	1	1	0	0	2	0	0	0	0	1	5	0	0	0
Intoxications	7	9	2	4	0	0	0	0	4	1	0	0	0	3	5	1	0	0
Septicemia	3	11	1	3	1	0	0	0	3	0	0	1	0	8	2	1	0	0
Dysentery	1	1	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
Typhoid fever	4	6	0	1	1	0	0	0	1	0	0	0	4	0	2	0	0	0
Other infections	5	5	1	0	1	0	0	0	2	0	0	0	0	3	1	1	0	0
Tuberculosis	3																	
Pneumonia	1																	
Balantidium coli	1																	
Diphtheria	1																	
Purpura hemorrhagica	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Benzol poisoning	0	0	0	0	0	0	0	0	0	0	0	0	5	0	2	1	0	0
Tumors (carcinomata)	5	5	1	2	1	0	0	0	1	0	0	0	0	2	3	0	0	0

*Probable. †(Approx.)

All blood, before transfusion, was tested in the majority of cases by Dr. Guthrie or his assistants. He has kindly given me the following directions for these tests:

DIRECTIONS FOR TESTING DONORS FOR TRANSFUSION.

1. From 2 to 5 cubic centimeters of blood are withdrawn by venapuncture and allowed to clot in a Wassermann tube.

2. One drop of blood is dropped into a test-tube containing

the development of iso-hemolysins. It is, therefore, most important that the bloods be matched before each transfusion.

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Case.	Age.	Sex.	Diagnosis.	Transfusion. Number.	Date.	Amount in c.c.	Method.	Reaction.	Blood Pressure. Before.
T. A.	38	M.	Pernicious anemia. Pyorrhœa alveolaris. Splenectomy.	1st	Mar. 9, 1915	700	Lindeman	None	?
				2d	Mar. 26, 1915	750	Lindeman	None	?
				3d	July 3, 1915	650	Lindeman	None	?
				4th	July 10, 1915	675	Lindeman	None	?
				5th	July 24, 1915	700	Lindeman	None	?
				6th	Aug. —, 1915	700	Lindeman	None	?
				7th	Aug. 27, 1915	700	Lindeman	None	100
				8th	Sept. 1, 1915	625	Lindeman	None	No
				9th	Sept. 3, 1915	675	Lindeman	None	?
				10th	Sept. 9, 1915	675	Lindeman	None	110
				11th	Sept. 11, 1915	880	Lindeman	None	110
				12th	Sept. 23, 1915	770	Lindeman	None	110
				13th	Oct. 7, 1915	675	Lindeman	None	120
P. B.	42	M.	Pernicious anemia	1st	Jan. 23, 1915	650	Lindeman	Severe reaction. Chill. Temperature 105°. Pulse 120. No hemoglobinuria or jaundice.	?
J. B.	43	F.	Pernicious anemia. Pyorrhœa alveolaris. Splenectomy.	1st	Sept. 25, 1915	800	Lindeman	Slight temperature reaction. No chill. Urticaria and itching. No hemoglobinuria.	125/7
				2d	Sept. 30, 1915	900	Lindeman	None	120/7
				3d	Oct. 9, 1915	900	Lindeman	None	?
				4th	Oct. 16, 1915	900	Lindeman	None	?
				5th	Oct. 24, 1915	20	Lindeman	Marked. Temperature 102°. Chill and hemoglobinuria. Second test of blood showed hemolysis and agglutination.	120/5
				6th	Oct. 30, 1915	900	Lindeman	None	?
				7th	Dec. 11, 1915	788	Lindeman	None	?
				8th	Dec. 14, 1915	900	Lindeman	None	?
				9th	Dec. 18, 1915	800	Lindeman	None	130/8
				10th	Dec. 21, 1915	280	Lindeman	None	135/1
				11th	Dec. 30, 1915	550	Lindeman	Temperature rose to 101.5°. Chill. Urticaria. No hemoglobinuria. No jaundice.	120/7
				12th	Jan. 22, 1916	500	Lindeman	None	?
				13th	Feb. 12, 1916	660	Lindeman	Temperature rose to 101.3°. No other reaction.	?
				14th	Feb. 14, 1916	270	Lindeman	None	?
H. P.	62	M.	Pernicious anemia. Splenectomy	1st	Jan. 12, 1916	200	Unger apparatus.	Temperature rose to 103°. Violent chill. Collapse. No hemoglobinuria. No hemolysis or agglutination.	?
				2d	Jan. 21, 1916	300	Lindeman	None	?
				3d	Jan. 24, 1916	682	Lindeman	Temperature rose to 101°. No other reaction.	?
				4th	Jan. 26, 1916	640	Lindeman	Temperature 100°. No other reaction.	...
				5th	Feb. 2, 1916	630	Lindeman	Patient vomited. Two urticarial lesions. No temperature reaction. No hemoglobinuria. Felt chilly. No chill.	...
				6th	Feb. 7, 1916	660	Lindeman	Temperature rose to 101.6°. Felt chilly. No chill. No other reaction.	...
				7th	Feb. 19, 1916	450	Lindeman	Temperature rose to 102°. No other reaction.	...
				8th	Feb. 26, 1916	360	Lindeman	None	...
				9th	Mar. 6, 1916	500	Lindeman	Temperature rose to 101°. Many patches of urticaria. No hematuria. Slight shaking chill. Patient not uncomfortable.	...
				10th	Mar. 13, 1916	450	Lindeman	Temperature rose to 100°. No urticaria or hematuria.	..
M. C.	54	F.	Pernicious anemia	1st	Nov. 17, 1915	250	Lindeman	Slight rise in temperature. No other reaction.	...
				2d	Dec. 5, 1915	320	Lindeman	Temperature rose to 101.6°. No other reaction. No hemoglobinuria.	...
N. D.	57	M.	Pernicious anemia. Hypertension	1st	Oct. 21, 1915	662	Lindeman	Severe chill. Temperature rose to 105.7°. Hemoglobinuria for 21 hours. Hemolysis and agglutination. Jaundice.	60/70

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
?	?	25	33	8	1,428,000	1,920,000	492,000	Incision for vein	Beneficial	1
?	?	54	67	13	2,128,000	2,440,000	312,000	Following this transfusion the patient was discharged from hospital.	Beneficial	2
?	?	29	40	11	840,000	1,656,000	816,000	Returned to hospital in poor condition (absent three months).	Beneficial	3
?	?	32	41	9	1,296,000	2,128,000	832,000		Beneficial	4
?	?	35	?	?	1,884,000	?	?	Splenectomy following transfusion	Beneficial	5
?	?	29	45	16	?	?	?		Beneficial	6
160	100	40	60	20	1,888,000	3,220,000	1,332,000	Interval of 11 days between blood counts	Beneficial	7
No change		50	60	10	1,960,000	3,088,000	1,128,000		Beneficial	8
?	?	60	70	10	3,088,000	3,144,000	56,000		Beneficial	9
110	132	60	65	5	2,424,000	?	?		Beneficial	10
110	130	65	75	10	2,424,000	3,688,000	1,264,000		Beneficial	11
110	130	80	85	5	3,632,000	4,432,000	800,000	Incision for vein	Beneficial	12
120	120	80	90	10	4,928,000	5,280,000	352,000	Jan. 17, 1916. Hb. 93%. Over three months without treatment.	Beneficial	13
?	?	25	39	14	960,000	1,680,000	720,000		No benefit	14
125/70	115/60	20	35	15	680,000	1,520,000	840,000		Beneficial	15
120/70	122/70	35	45	10	1,664,000	2,048,000	384,000		Beneficial	16
?	?	55	76	21	2,240,000	3,520,000	1,280,000	Following these transfusions patient says she feels "stuffed" and that the eyelids feel thick and swollen.	Beneficial	17
?	?	76	85	9	2,432,000	4,176,000	1,744,000		Beneficial	18
120/55	?	85	52	*33	4,176,000	2,672,000	*1,504,000	Marked decrease in R. B. C. and hemoglobin	Harmful	19
?	?	47	62	15	3,624,000	4,000,000	376,000	Patient discharged from hospital following this transfusion greatly improved.	Beneficial	20
?	?	22	40	18	648,000	2,158,000	1,510,000	Patient returned to hospital. Condition same as on first admission, poor. Absent 41 days.	Beneficial	21
?	?	42	55	13	2,450,000	3,158,000	708,000		Beneficial	22
120/80	170/100	?	?	?	?	?	?		Beneficial	23
135/100	?	?	48	?	?	3,000,000	?	Splenectomy Dec. 21, 1915. Transfusion 12 hours later.	Beneficial	24
120/72	142/85	53	48	5	1,900,000	?	?	No agglutination or hemolysis	No benefit	25
?	?	51	70	19	3,368,000	3,648,000	280,000	Two days between blood counts	Beneficial	26
?	?	74	78	4	3,792,000	?	?		Beneficial	27
?	?	78	82	4	?	?	?	Patient discharged	Beneficial	28
?	?	26	23	*3	1,224,000	1,440,000	216,000		Harmful	29
?	?	21	26	5	1,440,000	1,448,000	8,000		Beneficial	30
?	?	29	36	7	2,352,000	2,608,000	256,000		Beneficial	31
...	...	36	50	14	2,352,000	2,416,000	64,000		Beneficial	32
...	...	50	55	5	2,416,000	2,434,000	28,000		Beneficial	33
...	...	54	65	11	3,040,000	4,680,000	1,640,000	Feb. 12, 1916. Splenectomy	Beneficial	34
...	...	65	?	?	2,482,000	2,726,000	244,000		Beneficial	35
...	...	63	..	..	3,072,000	....	....		Beneficial	36
...	...	70	76	6	3,752,000	3,824,000	72,000		Beneficial	37
..	...	71	86	15	3,584,000	4,736,000	1,152,000		Beneficial	38
...	...	77	84	7	2,424,000	3,244,000	1,020,000	Spinal cord Ss. prominent	No benefit	39
...	...	77	?	?	3,472,000	?	?	Patient discharged	No benefit	40
160/70	160/75	31	35	4	1,280,000	1,208,000	*72,000	Three days later patient perfectly recovered. Hb. 30%. R. B. C. 1,208,000.	Harmful	41

*Lost.

Case.	Age.	Sex.	Diagnosis.	Transfusion.				Reaction.
				Number.	Date.	Amount in c.c.	Method.	
R. H.	..	M.	Pernicious anemia. Oral sepsis. Large spleen.	1st	June 22, 1915	610	Lindeman	Temperature rose to 105°. Brownish eruption on body. Hæmorrhagic areas on arms. Marked hemoglobinuria.
F. I.	44	M.	Pernicious anemia	1st	Mar. 25, 1907	1280*	Suture of vein to artery.	None
T. M.	54	M.	Pernicious anemia	1st	Dec. 9, 1915	638	Lindeman	None
R. M.	27	M.	Pernicious anemia. Cord changes	1st	Oct. 29, 1914	540	Lindeman	None
				2d	Nov. 14, 1914	500	Lindeman	Temperature 101° for 24 hours following transfusion. 48 hours later rose to 105°. Œdema of extremities. Râles in lungs. No hemoglobinuria.
L. O'F.	37	F.	Pernicious anemia	1st	May 24, 1915	660	Lindeman	None
E. W.	35	F.	Pernicious anemia. Splenectomy	1st	Feb. 3, 1914	?	Elsberg Cannula-Rachal artery to saphenous vein.	None
M. W.	55	F.	Pernicious anemia	1st	Oct. 23, 1915	750	Lindeman	Urticaria appeared 10 minutes after completion of transfusion. No other reaction.
S. H.	..	M.	Pernicious anemia. Splenectomy	1st	April 4, 1915	380	Lindeman	None
				2d	April 9, 1915	660	Lindeman	None
				3d	April 17, 1915	600	Lindeman	None
				4th	April 24, 1915	625	Lindeman	None
				5th	April 30, 1915	560	Lindeman	None
				6th	May 14, 1915	650	Lindeman	None
				7th	May 28, 1915	600	Lindeman	None
				8th	Aug. 22, 1915	..	Lindeman	None
				9th	Aug. 29, 1915	900	Lindeman	None
				10th	Sept. 11, 1915	726	Lindeman	None
				11th	Sept. 19, 1915	484	Lindeman	None
R. A.	45	M.	Chronic nephritis and myocardial insufficiency with secondary anemia.	1st	Feb. 26, 1915	550	Lindeman	None
H. A.	..	M.	Papilloma of bladder. Secondary anemia.	1st	Aug. 23, 1912	?	Direct transfusion. Artery to vein.	Temperature 101° following transfusion. No other reaction. Blood in urine continuously before transfusion.
N. B.	11	M.	Burns on legs. Secondary anemia	1st	Sept. 7, 1915	484	Lindeman	Temperature rose to 103°. No other reaction.
R. B.	1½ mo.	F.	Secondary anemia. Syphilis. Pneumonia. Otitis media.	1st	Nov. 18, 1915	110	Lindeman	Temperature rose to 101°. No other reaction.
I. B.	26	F.	Submucous sarcoma (uterus). Secondary anemia.	1st	Oct. 15, 1915	200	Lindeman	Vomited. Air hunger. Death. Patient was practically moribund prior to transfusion and operation. Tests showed no agglutination or hemolysis (?).
R. C.	20	F.	Chronic pelvic inflammatory disease. Secondary anemia.	1st	Feb. 12, 1915	300	Lindeman	Severe reaction. Vomiting. Collapse. Temperature 103.4°. Pulse 170. Chill.
H. C.	1	F.	Foreign body in intestine. Secondary anemia.	1st	Sept. 6, 1915	250	Lindeman	Temperature rose to 104°. No other reaction.
R. C.	2 mos.	F.	Secondary anemia	1st	Oct. 9, 1915	110	Lindeman	Temperature rose to 102°. No other reaction.
				2d	Oct. 30, 1915	115	Lindeman	
				3d	Jan. 21, 1916	100	Lindeman	
				4th	Feb. 24, 1915	160	Lindeman	
V. C.	26	M.	Brain tumor, cerebral, left. Secondary anemia.	1st	Nov. 4, 1914	600	Lindeman	None
W. D.	2 mos.	M.	Alimentary intoxication. Secondary anemia.	1st	July 27, 1915	30	Lindeman	None
N. H.	2	M.	Third degree burns, legs and body. Secondary anemia.	1st	Dec. 31, 1915	130	Lindeman	Temperature became subnormal. Child seemed worse.
O. H.	Baby	M.	Alimentary intoxication. Secondary anemia.	1st	Aug. 7, 1915	100	Lindeman	None
C. M.	9	M.	Splenomegaly. Secondary anemia	1st	May 10, 1912	?	Direct transfus'n. Radial artery to basilic vein.	None
A. P.	5	F.	Burns, abdomen and thighs. No anemia.	1st	Nov. 3, 1910	?	Direct transfus'n. Radial artery to vein.	None
H. R.	26	F.	Gastric ulcer. Chronic nephritis. Arteriosclerosis. Secondary anemia.	1st	Jan. 10, 1915	850	Lindeman	Vomited. Hemoglobinuria. Death.
R. S.	3	M.	Mongolian idiocy. Secondary anemia.	1st	Oct. 30, 1915	274	Lindeman	Temperature rose to 103.2°.
J. S.	22	M.	Congenital syphilis. Ulcer of legs. Secondary anemia.	1st	April 19, 1915	625	Lindeman	None
R. S.	2½	M.	Duodenal ulcer. Intestinal indigestion. Secondary anemia.	1st	Sept. 21, 1915	133	Lindeman	None

* Estimated.

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
?	?	34	35	1	1,430,000	?	?	During transfusion patient complained of nausea and pain in back.	Harmful	42
?	?	22	38	16	848,000	1,880,000	1,032,000	16 c. c. of blood collected from Radial in one minute at close of transfusion. Amount roughly estimated.	Beneficial	43
94/60	108/63	57	62	5	1,126,000	3,000,000	1,874,000	.....	Beneficial	44
?	?	21	34	7	1,024,000	1,584,000	560,000	.....	No benefit	45
?	?	35	39	4	1,504,000	1,800,000	296,000	Very atypical reaction.....	Harmful	46
?	?	44	56	12	1,672,000	2,272,000	400,000	Patient discharged	Beneficial	47
?	?	35	56	21	1,504,000	2,228,000	1,724,000	Splenectomy performed with transfusion in progress.	Beneficial	49
135/70	130/90	32	50	18	1,528,000	2,864,000	1,336,000	.....	Beneficial	50
?	?	22	27	5	1,200,000	?	?	.....	Beneficial	51
?	?	29	39	10	1,180,000	1,832,000	652,000	.....	Beneficial	52
?	?	37	43	6	2,016,000	2,408,000	392,000	.....	Beneficial	53
?	?	41	47	6	2,252,000	2,660,000	408,000	.....	Beneficial	54
?	?	46	55	9	2,552,000	2,960,000	408,000	.....	Beneficial	55
?	?	48	58	10	2,370,000	2,992,000	622,000	Splenectomy May 18, 1915.....	Beneficial	56
?	?	34	50	16	2,168,000	?	?	Lues	Beneficial	57
100	100	14	32	18	960,000	1,352,000	392,000	.....	Beneficial	58
124	124	33	46	13	1,352,000	?	?	.....	Beneficial	59
98	115	32	42	10	1,400,000	2,392,000	992,000	.....	Beneficial	60
105	112	33	42	9	1,480,000	1,880,000	400,000	.....	Beneficial	61
?	?	60	65	5	3,104,000	4,024,000	80,000	400 c. c. withdrawn from patient. 550 c. c. of blood from daughter injected.	Beneficial	62
?	?	18	39	21	?	?	?	.....	Beneficial	63
?	?	39	61	21	?	3,860,000	?	.....	Beneficial	64
?	?	14	38	24	?	2,712,000	?	Blood injected into external jugular vein.....	Beneficial	65
?	?	15	?	?	?	?	?	Uterus curetted and packed.....	Harmful	66
?	?	20	24	4	1,200,000	?	?	5 c. c. of vital red intravenously by Dr. Rowntree.....	Harmful	67
?	?	40	52	12	2,442,000	?	?	.....	Beneficial	68
?	?	15	58	43	?	?	?	Incision for vein at elbow.....	Beneficial	69
?	?	..	..	..	....	....	....	Blood injected into longitudinal sinus.....	Beneficial	70
?	?	..	..	..	....	....	....	Incision for vein.....	Beneficial	71
?	?	14	..	..	....	....	....	Given into vein on back of hand. Incision for vein...	Beneficial	72
115	?	45	55	10	2,680,000	3,800,000	1,120,000	Two operations prior to transfusion with much hemorrhage.	Beneficial	73
...	...	..	..	..	?	?	?	Injected into longitudinal sinus.....	No benefit	74
?	?	34	35	1	?	?	?	Injected into longitudinal sinus.....	Harmful	75
...	...	..	..	..	....	....	....	.....	No benefit	76
...	...	10	23	13	?	1,885,000	?	.....	Beneficial	77
?	?	90	93	3	4,600,000	4,500,000	100,000	Probably no blood given.....	No benefit	78
158/100	200/135	25	43	18	3,230,000	?	?	Patient vomiting blood prior to transfusion. Autopsy.	Harmful	79
?	?	18	55	37	768,000	2,768,000	2,000,000	Incision for vein.....	Beneficial	80
?	?	36	48	12	1,680,000	2,464,000	784,000	.....	Beneficial	81
?	?	40	40	0	?	?	?	Incision for vein.....	No benefit	82

Case.	Age.	Sex.	Diagnosis.	Transfusion.				Reaction.
				Number.	Date.	Amount in c.c.	Method.	
G. T.	6 mos.	F.	Acute intestinal indigestion. Secondary anemia.	1st	July 27, 1915	45	Lindeman	Severe. Temperature rose to 103.5° same night. To 105° next night and to 105° next. Death. No jaundice. No urinalysis.
B. T.	2 wks.	F.	Bleeding from umbilical cord stump. Secondary anemia. Syphilis (?).	1st	July 10, 1915	50	Lindeman	None
M. T.	54 yrs.	M.	Gallstone in common duct operation. Secondary anemia.	1st	April 3, 1915	520	Lindeman	Chill. Temperature rose to 103.8°. No hemoglobinuria.
H. M.	1½	M.	Hemophilia. Secondary anemia.	1st	June 8, 1915	100	Lindeman	None
				2d	Aug. 6, 1915	100	Lindeman	None
				3d	Aug. 10, 1915	254	Lindeman	None
				4th	Aug. 14, 1915	275	Lindeman	None
C. S.	24	M.	Hemophilia. Chronic arthritis.	1st	Sept. 4, 1915	66	Lindeman	None
E. H.	39	M.	Brain tumor. Operation. Hæmorrhage. Shock.	1st	Sept. 9, 1915	300	Lindeman	None as far as could be observed.
F. H.	16	M.	Rupture of kidney. Hæmorrhage. Shock.	1st	Jan. 10, 1912	?	Direct transfus'n. Crile clamp.	None
W. S.	19	M.	Typhoid fever. Second perforation. Hæmorrhage. Shock.	1st	Dec. 31, 1915	400	Lindeman	None
A. S.	25	F.	Colloid goitre. Hyperthyroidism. Operation. Hæmorrhage. Shock	1st	Nov. 14, 1915	420	Lindeman	None
T. C.	37	M.	Duodenal ulcer. Acute alcoholic gastritis. Hæmorrhage.	1st	Feb. 5, 1915	500	Lindeman	None
E. B.	2	F.	Leukemia	1st	Oct. 5, 1915	120	Lindeman	None immediately. Transfusion done at another hospital.
J. S.	31	M.	Acute myeloid leukemia. Bronchopneumonia. Adherent pericardium.	1st	Dec. 19, 1909	?	Crile-Bernheim Cannula. Artery to vein.	None
				2d	Jan. 2, 1910	?	Direct method. Crile Cannula. Artery to vein.	None
C. S.	7	M.	Acute leukemia	1st	May 16, 1913	?	Direct	Temperature rose to 103°. Râles in lungs. Cough. Dyspnœa.
G. W.	25	F.	Chronic myeloid leukemia. Hæmorrhagic diathesis.	1st	Nov. 30, 1915	520	Lindeman	Temperature rose slightly. Chill. No hemoglobinuria. No other reaction.
E. S.	26	M.	Splenomylogenous leukemia. Epistaxis. Secondary anemia.	1st	July 7, 1913	?	Direct transfus'n. Esmarch Cannula. Artery to vein.	None. Patient moribund when taken to operating room and died on the table.
J. B.	1	M.	Intestinal indigestion. Acidosis.	1st	Feb. 5, 1916	155	Lindeman	Temperature rose to 102.5°.
B. B.	32	F.	Chronic nephritis. Myocardial insufficiency. Secondary anemia. Uræmia.	1st	Nov. 11, 1914	600	Lindeman	Temperature 100°. Body and limbs itched for 24 hours. Some nausea. No hemoglobinuria.
				2d	Dec. 8, 1914	400	Lindeman	Temperature rose to 104.4°. Blood pressure fell 100 mm. Hg. Several convulsions.
				3d	Dec. 12, 1914	500	Lindeman	None
P. K.	21	M.	Chronic nephritis. Secondary anemia. Uræmia. Myocardial insufficiency.	1st	Jan. 22, 1916	600	Lindeman	Temperature rose to 102.5°.
M. P.	3 wks.	F.	Acute intestinal indigestion. Acidosis.	1st	Jan. 8, 1916	22	Lindeman	None
E. W.	34	M.	Chronic nephritis. Uræmia. Secondary anemia. Œdema lungs.	1st	April 21, 1915	500	Lindeman	Patient died a few hours later of pulmonary œdema.
J. M.	28	M.	Pyelonephritis. Cystitis. Septicemia.	1st	Dec. 2, 1914	240	Lindeman	Became restless, nervous, cyanotic, dyspnœic and died on table. Hemolysis.
G. R.	27	M.	Gonococcus septicemia. Acute nephritis. Endocarditis.	1st	Oct. 24, 1914	325	Lindeman	None
				2d	Oct. 31, 1914	600	Lindeman	None
C. S.	45	M.	Streptococcus septicemia	1st	Nov. 24, 1915	205	Lindeman	None
				2d	Dec. 11, 1915	220	Lindeman	None
				3d	Dec. 20, 1915	250	Lindeman	None
				4th	Jan. 7, 1916	200	Lindeman	Temperature rose 1°.
				5th	Jan. 26, 1916	176	Lindeman	Temperature reached 103°, but usual evening rise for this patient was to 102-103°.
				6th	Feb. 10, 1916	257	Lindeman	None apparently.
D. W.	20	F.	Bacillary dysentery (Shigo). Pulmonary tuberculosis.	1st	Oct. 30, 1915	800	Lindeman	Difficult to judge. Patient markedly jaundiced next day. Moribund when transfusion was done.
R. B.	24	M.	Typhoid fever. Relapse. Hæmorrhage. Otitis media. Cervical adenitis. Parotitis.	1st	May 21, 1915	600	Lindeman	Wonderful improvement. Temperature fell from 103° to 100.5°. Pulse from 140 to 108. Blood pressure rose 18 mm. Hg. Bleeding from intestine ceased.

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
...	...	..	..	..	....	....	....	Incision for vein—leg	Harmful	83
?	?	30	50	20	....	....	....		Beneficial	84
?	?	?	64	?	?	?	?	Patient bled slowly but steadily after operation. Transfusion caused no cessation.	No benefit	85
...	...	22	37	15	2,472,000	2,854,000	382,000	Patient bleeding from wound on tongue; ceased folfowing transfusion.	Life saving	86
...	...	?	35	?	?	?	?	Again bleeding. Ceased with transfusion	Life saving	87
...	...	28	55	27	?	?	?	Again bleeding. Suture of wound ineffectual several times.	Life saving	88
...	...	55	92	37	?	?	?	Wound healing	Life saving	89
?	?	80	?	?	?	?	?		No benefit	90
?	?	?	?	?	?	?	?	Patient moribund. Blood not tested for agglutination or hemolysis. Perhaps slight temporary benefit. Patient died in 18 hours.	No benefit	91
...	...	?	62	?	?	3,920,000	?		Beneficial	92
...	...	..	..	..	....	....	....	Patient died a few hours after transfusion and second perforation and operation.	No benefit	93
?	?	?	68	?	?	2,624,000	?		Beneficial	94
108/64	?	54	?	?	3,350,000	?	?	Patient vomited large amounts of blood. Operation. Ligature of bleeding vessel. Death two hours later.	No benefit	95
84	108	?	?	?	?	?	?	Patient died a few weeks later	No benefit	96
?	?	20	25	5	840,000	1,130,000	290,000	Patient bled from incision made for vein	No benefit	97
?	?	20	31	11	960,000	1,224,000	264,000	Patient oozed from incision made for veins. Hb. soon fell to former level.	No benefit	98
?	?	27	43	16	1,990,000	2,400,000	410,000	Patient died six weeks later	No benefit	99
?	?	30	37	7	2,432,000	2,756,000	324,000	Wound on back from which patient had oozed at intervals for 20 days and had not healed, ceased oozing and healed rapidly.	Beneficial	100
?	?	10	?	?	1,092,000	....	....		No benefit	101
...	...	..	..	..	....	....	....	60 c. c. of blood withdrawn and 155 c. c. injected	No benefit	102
...	...	38	52	14	2,984,000	3,996,000	112,000		Beneficial	103
...	...	46	45	*1	2,920,000	2,376,000	*544,000	Plasmaphæresis	Harmful	104
160	190	41	47	6	?	?	?	500 c. c. first withdrawn from patient, then 500 c. c. of husband's blood injected.	Beneficial	105
...	...	26	37	11	2,088,000	2,200,000	112,000	General condition improved	Beneficial	106
...	...	32	?	?	1,500,000	?	?	Injected into longitudinal sinus. Small cephalohæmatoma.	No benefit	107
...	...	..	..	..	....	....	....		Harmful	108
...	...	19	?	?	1,712,000	....	....		Harmful	109
100	108	22	26	4	?	?	?		Beneficial	110
105/65	118/80	23	30	7	1,650,000	2,150,000	500,000	No influence on septicema. Incision for vein	Beneficial	111
106	124	77	?	?	3,976,000	?	?		No benefit	112
94/65	94/75	77	78	1	3,328,000	?	?	Donor vaccinated with streptococcus causing septicemia in recipient.	No benefit	113
115/90	128/95	?	78	?	?	?	?	Same donor	No benefit	114
?	?	?	?	?	?	?	?	Same donor	No benefit	115
?	?	?	75	?	?	4,368,000	?	Blood cultures from patient showed no decrease in number of organisms.	No benefit	116
?	?	?	?	?	?	?	?		.....	117
?	?	65	?	?	5,672,000	?	?	Patient died 12 hours after transfusion	No benefit	118
80/40	98/60	45	51	6	?	?	?	Patient practically moribund prior to transfusion	Life saving	119

*Lost.

Case.	Age.	Sex.	Diagnosis.	Transfusion. Number	Date.	Amount in c.c.	Method.	Reaction.
R. B. ..... —cont.	24	M.	Typhoid fever. Relapse. Hæmorrhage. Otitis media. Cervical adenitis. Parotitis.	2d	May 25, 1915	700	Lindeman	Chill. Rise in temperature. Great improvement following. Temperature normal next day.
S. D.	27	M.	Typhoid fever. Perforation. Secondary anemia.	1st	Oct. 2, 1915	350	Lindeman	Temperature fell to normal 12 hours following transfusion. Then slowly rose to former level 102-103°.
E. S.	25	M.	Typhoid fever. Hæmorrhage. Secondary anemia.	1st	Nov. 13, 1915	460	Lindeman	Pulse fell from 120 to 104. Stopped bleeding from intestine. Temperature fell. Patient greatly improved.
				2d	Nov. 25, 1915	600	Lindeman	Pulse fell from 120 to 104 during transfusion. Temperature from 104.2° to 100° in next 12 hours. Stopped bleeding.
G. H.	7 wks.	F.	Diphtheria. Primary anemia...	1st	Nov. 4, 1914	60	Lindeman	Temperature rose to 103°. No other reaction. Temperature elevation commenced prior to transfusion. Probably no association.
E. K.	5	M.	Tuberculous enteritis. Secondary anemia.	1st	Dec. 29, 1915	350	Lindeman	None .....
C. L.	7	M.	Tuberculous splenomegaly	1st	May 14, 1914	?	Direct transfus'n.	None .....
H. W.	25	M.	Balantidium coli infection. Myocardial insufficiency. Secondary anemia.	1st	May 12, 1915	375	Lindeman	Temperature rose to 105°. Pulse 140. Collapse. No hemoglobinuria.
J. G.	44	F.	Purpura hæmorrhagica	1st	Aug. 31, 1915	330	Lindeman	None .....
F. C.	14	F.	Benzol poisoning	1st	July 8, 1909	?	Direct. Crile Clamp.	None .....
				2d	July 12, 1909	?	Direct. Crile Clamp.	None .....
S. H.	31	F.	Benzol poisoning	1st	May 3, 1914	?	Direct	None .....
				2d	May 17, 1914	?	Direct. Moss method.	Slight hemoglobinuria. No other reaction.
				3d	May 23, 1914	?	Direct	None .....
				4th	May 31, 1914	?	Direct	None .....
				5th	June 13, 1914	?	Direct	None .....
M. W.	14	F.	Benzol poisoning	1st	July 3, 1909	?	Direct	None .....
J. F.	53	F.	Carcinoma stomach. Metastasis. Thrombus of superficial veins. Secondary anemia. Cerebral embolus.	1st	Nov. 8, 1915	788	Lindeman	Violent chill, elevation of temperature. Pulse rose from 120 to 140.
J. J.	?	M.	Carcinoma prostate. Hæmorrhage. Secondary anemia.	1st	May 28, 1915	?	Lindeman	None .....
D. J.	60	M.	Carcinoma stomach. Secondary anemia.	1st	Dec. 9, 1913	?	Direct transfus'n. Crile Cannula.	None .....
P. M.	40	M	Carcinoma stomach. Abscess liver. Secondary anemia.	1st	July 3, 1915	600	Lindeman	Mild. Slight rise in temperature. No other reaction.
A. W.	..	F.	Carcinoma stomach. Metastasis. Secondary anemia.	1st	Sept. 9, 1915	484	Lindeman	Collapse. No temperature reaction. Soon rallied. No cardiac dilatation. No hemoglobinuria or jaundice.
H. P.	62	M.	Pernicious anemia (see this table, Reference Nos. 29-38).	11th	April 5, 1916	450	Lindeman	None .....
C. S.	45	M.	Streptococcus septicemia (see 112-117).	7th	Mar. 14, 1915	210	Lindeman	Temperature rose to 102.6°. Chilly sensation but no shaking. No hematuria.
				8th	April 1, 1916	220	Lindeman	Temperature rose to 108°. No chill. No hematuria.
				9th	May 1, 1916	264	Lindeman	No reaction.
T. D.	Baby.	F.	Bleeding from puncture wound on back.	1st	April 25, 1916	60	Lindeman	Temperature rose to 104°. Patient died nine hours afterward. No evidence of hypertransfusion.
J. W.	Baby.	M.	Acidosis following operation. Removal of omental cyst.	1st	April 21, 1916	47	Lindeman	Probably. No reaction from transfusion. Child died 10 hours later.
W. T.	54	M.	Pernicious anemia	1st	April 19, 1916	400	Lindeman	Temperature rose to 101.5°. Chill. Urobilin + guaiac 0 (urine).
C. M.	47	F.	Pernicious anemia	1st	April 18, 1916	330	Lindeman	Patient's temperature became subnormal then rose to 99.5°. Urobilin +, guaiac negative (urine). Patient died nine hours after transfusion.
D. B.	55	M.	Pernicious anemia. Combined sclerosis. Splenectomy.	1st	April 8, 1916	440	Lindeman	None .....
E. C.	28?	F.	Typhoid fever. Pneumonia.....	1st	Mar. 30, 1916	496	Lindeman	Patient complained of pain in back after transfusion. Died nine hours later. Moribund when transfused.
B. A.	Baby.	..	Bleeding from umbilical cord....	1st	Mar. 24, 1916	50	Lindeman	None .....
R. C.	..	F.	Primary anemia (see Nos. 69-72)	5th	Mar. 21, 1916	140	Lindeman	.....
J. N.	Baby.	..	Malnutrition. Intoxication	1st	Mar. 14, 1916	130	Lindeman	Died five hours after transfusion. No evidence of hypertransfusion.

Blood Pressure.		Percentage of Hemoglobin.			Red Blood Cells.			Remarks.	Result.	Reference No.
Before.	After.	Before.	After.	Change.	Before.	After.	Change.			
118/72	?	38	46	8	?	?	?	Donor had had typhoid fever. Great improvement....	Life saving	120
130/70	?	40	48	8	?	?	?	Patient died two hours later. Autopsy.....	Beneficial	121
...	...	28	..	..	....	....	....	.....	Life saving	122
...	...	26	32	6	?	2,104,000	?	Incision for veins.....	Life saving	123
...	...	20	28	8	?	?	?	Injected into jugular vein (incision).....	Beneficial	124
?	?	?	36	?	?	2,400,000	?	24 hours later Hb. was 54%.....	Beneficial	125
?	?	35	60	25	?	?	?	Splenectomy later. Uneventful convalesence.....	Beneficial	126
?	?	16	20	4	?	?	?	Incision for vein.....	Harmful	127
?	?	75	?	?	4,064,000	?	?	No benefit. Patient died soon after leaving hospital of cerebral hemorrhage.	No benefit	128
?	?	28	28	0	2,128,000	2,160,000	*32,000	Transfusion not successful.....	Harmful	129
?	?	15	?	?	1,150,000	?	?	Transfusion not successful. Patient died short time later. Autopsy.	Harmful	130
?	?	20	38	18	1,226,000	1,680,000	454,000	Patient greatly improved. Bleeding ceased temporarily.	Life saving	131
?	?	28	48	20	1,117,000	1,971,000	864,000	May 14, 1914. 500 c. c. of defibrinated blood by Dr. Moss' method.	Life saving	132
?	?	20	40	20	910,000	1,856,000	946,000	Patient bleeding from m. m. except immediately after transfusions.	Life saving	133
?	?	24	42	18	?	?	?	Donor not tested for agglutination or hemolysis.....	Life saving	134
?	?	48	65	17	3,476,000	4,528,000	1,052,000	Patient has practically ceased bleeding. Regenerating. Perfect recovery.	Life saving	135
?	?	11	8	*3	544,000	640,000	96,000	Transfusion unsuccessful	Harmful	136
97/56	100/58	25	30	5	2,800,000	?	?	.....	No benefit	137
?	?	15	30	15	?	2,160,000	?	.....	Beneficial	138
?	?	34	50	16	?	?	?	Gastro-enterostomy and partial resection while transfusion was done.	Beneficial	139
?	?	30	42	12	2,592,000	3,553,000	961,000	.....	Beneficial	140
?	?	?	?	?	?	?	?	.....	No benefit	141
...	...	82	88	6	3,272,000	3,640,000	68,000	Second transfusion from this donor.....	Beneficial	142
?	?	?	67	?	?	?	?	Temperature rises less every P. M. than upon admission.	Beneficial (?) ...	143
?	?	73	?	?	?	?	?	Patient's condition improving.....	Beneficial (?) ...	144
?	?	57	70	13	?	?	?	Blood cultures in Nov., 1915, showed 50 colonies to c. c. April 21, 1916, 2 colonies.	Beneficial (?) ...	145
?	?	?	?	?	?	?	?	Reaction strongly suggested an agglutination and hemolysis.	Harmful	146
...	...	..	..	..	....	....	....	Moribund when transfused.....	No benefit	147
...	...	47	57	10	1,648,000	?	?	.....	Beneficial	148
?	?	20	29	9	960,000	?	?	Patient moribund and with air hunger when transfused.	Harmful	149
?	?	85	100	15	3,048,000	3,952,000	904,000	Splenectomy on March 1, 1916.....	Beneficial	150
?	?	?	?	?	?	?	?	Transfusion done at home of patient.....	Questionable	151
?	?	?	?	?	?	?	?	Bleeding ceased. All other methods ineffectual.....	Beneficial	152
?	?	..	..	..	....	....	....	.....	Beneficial	153
?	?	?	?	?	?	?	?	.....	No benefit	†154

*Lost.

† In final balance one case must be subtracted (48 is vacant) making a total of 153 transfusions.

ALEUCOCYTHÆMIC LEUKÆMIA.

1. ACUTE MYELOBLASTIC LEUKÆMIA. 2. CHLOROMA (?). 3. CHRONIC LYMPHATIC LEUKÆMIA.

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In 1845 Hughes Bennett reported a case of a disease which he later called "leucocythæmia," or "white cell blood." Shortly after Bennett's publication, Virchow described a condition to which he gave the name "leukæmia," or "white blood."[1] The diseases recorded by these two observers were undoubtedly identical in nature, but "leukæmia" has gained general recognition as the name of this disease entity. In its etiological sense, however, neither term is always descriptive of the disease. There are instances of true leukæmia (as the name is now used) in which there is no increase of leucocytes in the circulating blood; hence "leukæmia" has come to be used as the name of the disease as a pathological condition, regardless of the leucocyte count. In describing cases of true leukæmia without leucocytosis of the blood, the term "aleukæmic leukæmia" is frequently used, or the expression "leukæmia in the aleukæmic state," or "stage." "Aleukæmic" here is used in its etiological sense, indicating an absence of leucocytosis of the blood, whereas "leukæmia" is used in its derived sense, to indicate the fundamental pathology of the disease. To use two words of the same origin together and give them entirely different meanings creates a paradox that is often confusing. The confusion is increased by the fact that the word "aleukæmic" is used not only to describe conditions in which there is no leucocytosis, but also conditions which are "aleukæmic" because they bear no relation to leukæmia.

Waterhouse[2] has reported cases of true leukæmia with qualitative blood changes but which showed no increase in the total number of white blood cells. "Aleucocythæmic Leukæmia" is the title of his communication. This expression is not confusing, for the word "leucocythæmia" has retained its original significance, indicating an increase of white blood cells in the blood; moreover, it has its source in the original report of Bennett.

It is now well known that the number of leucocytes in the blood in true leukæmia may be normal or even subnormal. One or more of a variety of circumstances may be responsible for this condition. As the result of treatment with X-rays, arsenic, benzol, etc., the leucocytes not infrequently drop to a normal total count. Indeed, care must be taken in using these therapeutic agents to avoid too great a suppression of the leucocytes. Intercurrent infections, such as influenza, typhoid fever, tuberculosis and septicæmia, may cause a reduction of the leucocytes in leukæmia. There are certain cases of leukæmia in which the leucocyte count may be normal during some stage of the disease, and others in which there probably never is a leucocytosis. Incipient cases are most apt to present a normal white cell count, but the same may occur in the terminal stage or during the course of the disease.

In most of the above cases a differential count would be expected to show an abnormal blood picture, usually with definitely immature cells. In such cases there is no doubt about the diagnosis of leukæmia. There is, however, a small group of cases to which the name "pseudoleukæmia" has been given by certain German writers. In these cases, the pathology is that of leukæmia, except that the blood picture is normal. In many instances, this condition passes into one of undoubted leukæmia, with characteristic blood changes. The attempt to create a separate disease entity of such cases of pseudoleukæmia has not met with general acceptance, as the difference between these conditions and leukæmia is slight.[3]

The Pappenheim school points out the advisability of sharply differentiating cases of aleukæmic (aleucocythæmic) disease of the leucoblastic tissues from infectious granulomatous disease of this system and from lymphosarcoma and true tumors. They say, however, that the real hyperplastic pesudoleukæmia is only a particular form of chronic lymphadenoid leukæmia, and that the so-called medullary aleukæmic pseudoleukæmia shows the same diffuse changes in the bone-marrow as does the outspoken lymphadenoid leukæmia. Naegeli[4] holds the same conception, and considers that aleukæmic lymphadenosis and myelosis (pseudoleukæmia or aleukæmia) should fall into the group of leukæmias. In brief, it may be said that the conditions classified by various authors as true pseudoleukæmia, either lymphatic or medullary, as aleukæmia, as aleukæmic lymphadenosis or myelosis, and as aleukæmic leukæmia, are probably all to be considered leukæmia at an aleucocythæmic stage.

Other cases which can be differentiated by the history only from the group just described are those of leukæmia in remission. It is said that, in certain cases, remissions occur during which the blood picture may become perfectly normal. In some cases, the blood, spleen and all other tissues, so far as can be determined, may become perfectly normal during a remission.[5]

Chloroma is now generally recognized as a type of leukæmia characterized by green nodules, which have a predilection for for the periosteum of certain bones. Cases of chloromatous leukæmia, according to Naegeli, are more apt to present "anæmic, aleukæmic and sublymphæmic" blood pictures than are other forms of leukæmia. Naegeli explains this fact by the

[1] Osler, Sir Wm.: The Principles and Practice of Medicine, 1912.

[2] Waterhouse, R.: Bristol Med. and Chir. Jour., 1913, XXXI, 10.

I wish to acknowledge with thanks the work of Mr. Martin of the Phipps Psychiatric Clinic in making photomicrographs of the blood.

[3] Pappenheim, Baumgarten and others. Folia Hæmat., 1906, 453.

[4] Naegeli, O.: Leukämie u. Pseudoleukämie, 1913.

[5] Cabot, R. C.: Modern Medicine, Osler and McCrae, 1915.

hypothesis that the abnormal swelling of the chloroma tissue cells may prevent these cells from following the normal channels of passage into the blood stream. Only two cases are recorded, however, in which the aleucocythæmic condition of the blood persisted throughout the course of the disease. One is that of Bramwell,[6] which ran a febrile course, with a lethal ending one month after the patient came under observation. The white cell count was never increased, although 95% or more were lymphocytes, chiefly large lymphocytes. Türk[7] reported the other instance: this was a rapidly fatal case of chloroma, with a W. B. C. count between 2000 and 4100 per c. mm. There was a large lymphocyte percentage. The diagnosis was confirmed at autopsy.

In the records of The Johns Hopkins Hospital are 105 cases of leukæmia, of which 41 belong to the lymphatic, 64 to the myeloid variety. Five of the lymphatic leukæmia group were aleucocythæmic at some time. In one case the W. B. C. count fell from 33,500 to 1900 as a result of treatment with Fowler's solution, and the differential count became almost normal. Another case had a febrile course very similar to that of typhoid, during which the W. B. C. rose from 4300 to 16,800 (77.75% monos.). At discharge the blood presented a picture of chronic leukæmia—W. B. C. 5880, monos. 60.66%. A third case showed a fall of W. B. C. from 17,000 (large monos. 76.5%) to 6880 (64.5% monos.) following X-ray treatment and Fowler's solution. Another was a case of chronic aleucocythæmic lymphatic leukæmia or lymphadenosis, with a leucocyte count from 7200 to 9360, and the lymphocytes as high as 88.5%. Of the myeloid leukæmia cases, nine were aleucocythæmic at some stage. One acute case showed a normal total white cell count for a few weeks, while there were 73% myeloblasts. A few weeks before death there was, however, a flooding of the blood with white cells. Eight chronic myeloid cases were aleucocythæmic at some stage, five as the result of treatment, three spontaneously. No cases of chloroma are recorded.

During the past year three cases of leukæmia of the aleucocythæmic variety were studied at this hospital. In one of them an acute myeloblastic leukæmia, so far as is known, there was never a real leucocytosis; in the second, a case of chloroma, there was a history of a leucocytosis, but none was found in counts made several months apart; and in the third case, one of chronic aleucocythæmic lymphatic leukæmia, there was no leucocytosis prior to the terminal stage.

CASE.—Acute myeloblastic leukæmia. White school-girl, æt. 14.

Complaint.—Weakness.

Family History.—Negative, except for paresis in the father.

Past History.—Healthy girl. Two light attacks of scarlet fever, in infancy and at six years. Measles twice, at 10 and 12 years of age.

Present Illness.—The onset was three months before admission, with stiffness in the knees and pain on walking. Salicylates were ineffectual. No other joints were involved, but the pain in the knees continued until one month before admission. There was progressive pallor and weakness. One small hemorrhagic spot was seen on the left arm. There was no œdema nor dyspnœa. She lost 15 pounds in weight. Both the patient and her mother noticed some fullness of the abdomen. One week before admission a consulting physician found the W. B. C. count 8000.

Examination on Admission.—The skin and mucous membranes were very pale. Nothing unusual was noticed as to the gums and tonsils. There were enlarged glands at the angles of the jaws, and firm, palpable posterior cervical glands; these glands were only moderately enlarged. The axillary glands were palpable, but neither large nor soft, and the inguinals were not felt. There was some retromanubrial dullness. The spleen was notched and reached to a level two finger-breadths above the left anterior superior spine, and just beyond the umbilicus on the right. The liver edge was just below the costal margin. There was a small cutaneous hemorrhage on the left arm, and hemorrhages in both retinæ. An ankle clonus was obtained on the right side.

The Blood.—Bleeding time was definitely prolonged. Resistance of R. B. C. to hypotonic salt solutions was normal. There was marked anisocytosis and poikilocytosis of the red cells. R. B. C. 1,552,000. Hb. 25%. W. B. C. 7120.

Differential count (250 cells), Wilson stain:

Poly. Neut.	22.4	per cent.
Poly. Eosin.	0.4	"
Poly. Baso.	0.4	"
Large Mono.	0.4	"
Small Lymphocytes	0.4	"
Large Lymphocytes	1.2	"
Transitionals	0.0	"
Myeloblasts	57.6	"
Promyelocytes	1.6	"
Myelocytes (Neut.)	1.6	"
Myelocytes (Eosin.)	0.0	"
Myelocytes (Baso.)	0.4	"
Normoblasts	3.2	"
Intermediates	1.6	"
Megaloblasts	1.2	"
Smudges	6.4	"
Unclassified	1.2	"
	100.0	per cent.

The predominating cell was a typical, large myeloblast. The protoplasm was not granular, stained rather deeply basophilic, and was frequently vacuolated. The protoplasm was often extremely scanty. It was sometimes even darker than the nucleus. The nuclei were usually round oval, often with an incisure; they stained less deeply than the average lymphocyte nuclei, and showed a very delicate reticulation.

The Wassermann reaction was negative. The urine was negative: it showed no Bence-Jones proteinuria. The temperature varied from 99.5° to 100.6° F.

The patient left the hospital after two days' observation. She became worse and died, three months after the onset of the first symptom. Her physician wrote that the spleen just before death was about one-half its previous size; no further blood-counts were made. No autopsy was done.

The case is a typical one of acute myeloblastic leukæmia, except for the aleucocythæmic blood condition. The counts prior to the patient's admission and while she was in the hospital were not elevated, and although no counts were made after her discharge, it seems unlikely that an increase of white cells would have coexisted with a decrease in the size of the spleen.

CASE II.—Chloroma. White woman, æt. 58, widow, housewife.

Complaint.—Tenderness of the teeth. Puffiness of the eyes.

Family History.—Negative.

[6] Bramwell, B.: Brit. Med. Jour., 1902, I, p. 453.

[7] Türk, W.: Wien. klin. Wchnschr., 1903, XVI, 1023.

Past History.—Usual childhood diseases. Scarlet fever at five years, followed by difficulty in hearing.

Present Illness.—Four years before admission, the patient consulted a physician for indigestion. Through routine examination, an enlarged spleen was found. At that time, the W. B. C. were 18,000, with 85 per cent of small round cells. Since that time, counts have varied between 9000 and 30,000, with mononuclears between 65 per cent and 90 per cent. The spleen was treated with X-ray, and arsenic was given. A little more than two years before admission, a swelling was noticed on the left cheek, just anterior to the ear. Soon a tumor appeared above the right clavicle. For several months at that time there was severe pain in the legs, especially in the knees. One dose of Salvarsan was given. About six months before admission several swellings appeared in the neck on both sides, and subsequently the other masses described in the examination developed. A few months before admission, there was excruciating pain in the teeth. Several teeth were extracted, some abscesses were found, and there was relief from pain in the teeth and knees. The patient's friends noticed that her complexion was becoming yellowish-gray. At the time of admission she had no especial complaint. She had lost 30 pounds in weight. Her hearing had become much less acute, though always impaired since scarlatina.

Physical Examination.—The skin was dusky, with an olive tint. There were masses on both malar eminences, invading the eye sockets. One of these masses measured 10 x 5 cm., and it was difficult to prove its connection with the bone. The other was smaller, firmer, and definitely attached to the bone. There was a flat mass connected with the left mastoid bone and extending downward to join matted nodules on the left side of the neck. She could hear nothing less than a shout. There was considerable thickening of the middle of the left clavicle. Glands were felt in the right and left axillæ; in the latter was a mass as large as the end of the thumb. Over the front of the chest were several subcutaneous nodules, to two of which the skin was attached. The inguinal glands were a little large on the left, not on the right. On the back were a number of small nodules, most of them in the skin. The surface of some of these had a somewhat grayish-brown color at the points where they were nearest the skin. They looked rather like old, discolored ecchymoses.

The gums were very tender about some of the exposed teeth. The heart and lungs were normal.

The liver reached to the umbilicus in the median line, and well below it on the right. The border was sharp and the surface smooth, with slight rounded prominences. The spleen reached about 7 cm. below the costal margin, was very firm and rather prolapsed toward the left.

Nothing abnormal was seen in the eye-grounds.

The Blood.—

Hgb. (Sahli) .....66 per cent.
R. B. C.....3,928,000
W. B. C.....5120

Differential Count.—

	Wilson Stain.		Ehrlich Stain.	
	No. Counted.	%	No. Counted.	%
Poly. Neut.	254	63.25	382	63.70
Poly. Baso.	0	0.00	1	0.17
Poly. Eosin.	23	5.75	34	5.60
Small Lymph.	62	15.50	128	21.30
Large Lymph.	33	8.25	41	6.80
Large Mono.	20	5.00	10	1.70
Transitionals	0	0.00	4	0.70
Neut. Myelocytes (?)	6	1.50	0	0.00
Myeloblasts (?)	2	0.50	0	0.00
	400	99.75	600	99.97

There was slight anisocytosis of the red blood cells, no poikilocytosis, and neither basophilia, punctate or diffuse, nor nucleated forms. The polymorphonuclear forms frequently showed coiled, elongated nuclei, not unlike rare transitional forms. The convolutions of the nuclei were seen most clearly in preparations poorly (lightly) stained by Ehrlich's method. Some of the nuclei resembled tightly coiled snakes, and in some of them one end of the nucleus was separated from the coil and seemed actually to protrude from the cell. In some instances a very tightly coiled nucleus looked very much like a mononuclear cell, especially in a Wilson-stained preparation.

The Wassermann reaction was negative. The urine was negative and showed no Bence-Jones protein.

A few months prior to her admission the patient's physician sent a bit of tissue, containing a subcutaneous nodule from her body, to this hospital for diagnosis. A laboratory assistant made a section and destroyed the gross specimen; the stained section was forwarded to Dr. Winternitz who was away. His report follows:

"The section is from subcutaneous tissue, and bits of degenerated voluntary muscle occur between the lobules of tumor mass. The lobules are irregular in size and shape, and, as far as can be determined, do not represent a change in a preëxisting lymphoid structure but a new formation. This assumption is strengthened by the fact that several minute tubular structures occur in the very center of several lobules. These tubular structures are built by cubical epithelium and are only explainable by assuming that the tumor has infiltrated the deeper layers of the skin and surrounded some of the small glands and ducts, *i. e.*, the sweat-ducts of the skin.

Otherwise the tumor has a uniform appearance and consists almost entirely of a densely packed mass of small round cells similar to lymphocytes. In many places these overshadow the supporting framework of connective tissue and vessels completely.

In view of the history I should rather incline to regard this as a type of lymphatic leukæmia tending toward the aleukæmic variety with a tendency to nodule formation such as occurs in chloroma, mycetoma, etc. An absolute differentiation is, however, impossible from the section alone."

The patient left the hospital in the latter part of October, 1915, after two days' stay, and was again seen on April 2, 1916. In the interim she had had 36 injections of sodium cacodylate and eight X-ray treatments, one to the left side of the forehead, two to the back and the rest to the long bones. She had felt very well and had been quite active. Her chief complaint was of a neuralgic pain in the lower jaw.

Examination (April 2, Dr. Thayer).—The color was much better. The prominence which had been present on the left temple when last seen was entirely absent. There was still a slight prominence on the right forehead. The masses in the neck were about as before, but many of the nodules on the back had entirely disappeared. There were several nodules on the front of the chest. Although several of these were adherent, no definite discoloration of the skin could be made out. Three superficial masses in the skin, one just below the left breast and two below the right breast, showed a distinct slightly dirty gray-brown discoloration, just like that which was seen in the back on the previous examination.

The heart and lungs were clear.

The spleen was just about as before. The epitrochlear glands were palpable, the inguinals not essentially enlarged. The liver extended 12 to 12.5 cm. below the costal margin in the right mammillary line.

The patient's hearing was much improved. She could hear ordinary conversational tones.

The blood at this time showed:

Hb. (Sahli) .....80 per cent.
R. B. C.....4,000,000 (+)
W. B. C.....7000 (+)

Differential Count (Wilson Stain), 200 Cells.—

Poly. Neut.	54.0	per cent.	
Poly. Baso.....	1.0	"	R. B. C.: Slight anisocytosis. No poikilocytosis. No basophilia.
Poly. Eosin.....	6.5	"	
Large Mono.....	5.0	"	
Small Mono.....	27.5	"	Polymorphonuclears with convoluted nuclei again present.
Large Lymphocytes.	2.5	"	
Transitionals	2.5	"	
Myelocytes (Eosin.).	0.5	"	
Unclassified	0.5	"	
	100.0	per cent.	

The history of chronic splenomegaly, with leucocytosis and mononucleosis, the glandular enlargement and the many nodules of leucoblastic tissue left little doubt that the case was one of leukæmia. Certain features made the diagnosis of chloroma probable.

Chloroma is more common in individuals younger than this patient. The average age is about 20. Fifty-two years is the greatest age found reported. The onset of the disease is usually acute, often with pains in the knees, teeth or head. Hemorrhages, weakness and anæmia follow rapidly. Ulcerated gums and throat may lead to the diagnosis of Vincent's angina or diphtheria. There is usually exophthalmos, from invasion of the orbits by the chloroma tissue. Tumors form, showing a predilection for the periosteum of certain bones, especially of the face and skull. The order of frequency with which these bones are involved is: (1) Orbits. (2) Dura or sinuses. (3) Temporal bone. (4) Temporal fossa. (5) Sphenoid. (6) Ethmoid, etc. The nodules may be attached to sternum, ribs, lymphatic system, spleen, liver, subcutaneous tissue or kidneys. Pathological examination shows that there is practically no tissue or organ of the body which may not be infiltrated by chloroma tissue. The gross color of the nodules and of the infiltrating tissue is green. Sections of the tissue show lymphocytes and cells having the appearance of myeloblasts.[8] The most characteristic blood cell has been described by Butterfield,[9] and was thought by some to be pathognomonic of cases of chloroma, but it has often been seen in other cases of leukæmia. It is a non-granular mononuclear cell with a convoluted nucleus—a myeloblast. In cases of chloroma there are usually an enlarged spleen and liver. The course is almost always febrile, ending fatally in a few months. The longest case recorded lasted one and one-half years.

The case reported here was typical in the following respects: (1) The early pains in the teeth and knees. (2) The location of the tumors. (3) The color of the skin over the tumors, and the generalized olive tint. (4) The enlarged spleen, liver and lymphatics. (5) The anatomical appearance of the excised nodule. (6) The anæmia. (7) The convoluted nuclei of the polymorphonuclear cells may have some diagnostic significance. The case was unique in these features: (1) The patient's age (58). (2) The chronicity of the disease (now four years). (3) The almost normal blood picture.

There are eight chief hypotheses as to the nature of chloroma. They embody two main ideas—one that it is purely a leukæmic disease, and another that it is purely sarcomatous. Various combinations of these central ideas have been advanced, into which it is scarcely necessary to enter at length. These various hypotheses are discussed by Lehndorff,[10] from whom Pappenheim's views are quoted as follows: "Chloroma is a green-colored type of malignant hyperplasia of the hematopoietic tissue, which appears as hyperplastic chloroma or as chlorosarcoma, with all stages of intermediate forms."

It seems likely that the case reported here has more the nature of a neoplasm than of a blood disease; however, in view of the history of leucocytosis and mononucleosis, it seems not improbable that the case was studied during a remission and that definite leukæmic blood changes will appear before the disease has run its course.

CASE III.—Chronic Lymphatic Leukæmia. White man, aet. 60, married, farmer. Admitted April 3, 1916.

Complaint.—Indigestion. Weakness.

Family History.—Negative.

Past History.—Measles and pertussis in childhood. Pneumonia at 10. Erysipelas 10-12 years ago.

Present Illness.—In March, 1915, one year ago, he had an attack of "grippe" which lasted from six to eight weeks. He felt "weak and achy" until June. The skin became very tender and boils developed from the slightest injury. There was dyspnœa, which gradually increased until the time of admission. For three months before his admission, the patient had constant indigestion, without vomiting. He said he had had lumps under the left arm for 10 or 12 years. About six or eight months ago he noticed lumps in the neck, and in both groins about four months ago. He lost 30 to 40 pounds in weight. There was no œdema, and no purpura. There were many small boils from time to time, which ruptured and discharged bloody material.

Physical Examination (on admission).

There was marked emaciation. The skin was sallow, but lacked a lemon-yellow tint. There were a few pustules. The mucous membranes were quite pale. There was an occasional rather metallic cough, suggestive of mediastinal pressure. The teeth were very bad, many were carious, and there was a moderate pyorrhœa.

Glands.—The cervicals on both sides were enlarged, soft, discrete, and about the size of unshelled almonds. The axillaries were of similar consistency, but large—about the size of walnuts. The inguinal and epitrochlear glands were similar to the cervicals. In the right iliac fossa several rounded masses could be felt, which were thought to be glands.

Thorax and Heart.—Nothing unusual was found, except a rather loud systolic murmur at the heart's base, best heard over the right carotid artery. There was diffuse thickening of the radial vessels.

[8] Burgess, A. M.: Jour. Med. Research, 1912, XXII, 133.
[9] Butterfield, E. E.: Deutsch. Arch. f. klin. Med., 1908, XCII, 336.
[10] Lehndorff, H.: Jahrb. f. Kinderheilk. u. Phys. Erzieh., 1910, LXXII, 53.

Liver.—This was felt three fingerbreadths below the costal margin in the midclavicular line; its edge was sharp but the consistency of the organ was about normal.

Spleen.—The spleen was felt deep in the flank, presenting a sharp edge and a notch. It moved with respiration, and lay two to three fingerbreadths below the costal margin.

The Blood.—The flow and clotting are normal.

R. B. C.	3,128,000
Hb.	43 per cent.
W. B. C.	7720

Differential Count (Wilson Stain), 250 Cells.—

Poly. Neut.	37.6	per cent.
Poly. Baso.	0.8	"
Poly. Eosin.	3.2	"
Large Mono.	5.2	"
Small Lymphocytes	50.0	"
Transitionals	2.4	"
Large Lymphocytes	0.0	"
Large Mononuclears with convoluted nuclei and granular protoplasm	0.8	"
	100.0	per cent.

Slight anisocytosis and poikilocytosis of R. B. C. No basophilia nor nucleated forms.

Ewald Test Meal.—Negative except that there was seven per cent acidity deficit of free HCl. Total acidity was 20 ac. per cent.

Stool.—Negative.

Wassermann Reaction.—Negative.

Urine.—(Admission). S. G. 1.010. Alb. ++. Many pus cells. No blood. No casts.

Subsequently the pus disappeared from the urine, and the albumin was reduced to a trace.

April 8. X-ray treatment to spleen.

April 15. X-ray treatment to external glands.

April 17. W. B. C. 12,880.

Differential Count (Wilson Stain), 200 Cells.—

Poly. Neut.	59.0	per cent.
Poly. Baso.	0.5	"
Poly. Eosin.	1.0	"
Large Mono.	9.5	"
Small Lymphocytes	29.0	"
Transitionals	0.5	"
Myelocyte	0.5	"
	100.0	per cent.

Many of the cells classed as polymorphonuclears have convoluted nuclei.

April 20. Temp. 103° F. Cough. Congestion of lung bases. Hb. 44 per cent. R. B. C. 3,224,000. W. B. C. 21,500.

April 23. W. B. C. 16,080.

Differential Count (Wilson Stain), 200 Cells.—

P. M. N.	50.5	per cent.
P. M. B.	0.0	"
P. M. E.	0.0	"
Large Mono.	7.0	"
Small Lymph.	30.5	"
Large Lymph.	5.0	"
Transitionals	7.0	"
	100.0	per cent.

Many polymorphonuclear cells have thick, tightly or loosely coiled nuclei and neutrophilic granules. Some nuclei are snake-like and so closely coiled as to suggest a mononuclear cell. Others have thick and elongated nuclei resembling transitionals.

April 25. X-ray treatment to external glands. The glands are all smaller than on admission, but at present are not quite so soft in the center as they were just after the first treatment.

April 27. Marked diarrhœa. Stools contain pus, no blood.

Stool Culture.—Hiss-Russell dysentery bacilli obtained. W. B. C. 36,080.

April 29. Some vomiting. W. B. C. 30,350.

Differential 200 Cells.—

P. M. N.	41.0	per cent.
P. M. B.	0.0	"
P. M. E.	0.0	"
Large Mono.	0.5	"
Small Lymph.	58.0	"
Transitionals	0.5	"
	100.0	per cent.

April 30. Dysentery and vomiting continue. Irregular, sharp elevations of temperature (highest 102.6° F.) alternate with subnormal temperature. Dilatation of the stomach has set in. Definite "air hunger" to-day. CO_2 tension of alveolar air 22 mm. Hg.

May 1. Patient died.

The temperature ranged between 96° and 101° F. prior to the acute pulmonary infection of April 20.

Treatment.—X-rays to glands and spleen, Fowler's solution, Blaud's pills, hydrochloric acid, and special treatment for dysentery and pulmonary symptoms.

An autopsy was done, and Dr. H. C. Schmeisser gave the following report, with plates:

Autopsy No. 4677. *Anatomical Diagnosis.*—

Primary.—(1) *Lymphatic leukæmia involving particularly lymph-glands and parenchymatous organs.*

(2) *Acute necrotizing and ulcerative colitis (Hiss Bacillus).*

Subsidiary.—Gastric ulcer. Fibrous pleurisy (rt.); pulmonary emphysema. Aplasia of left renal artery and atrophy of left kidney (congenital).

The *body* is that of a large-framed, emaciated, white man, 180 cm. in length. There is marked anæmia of the conjunctivæ, lips and tissue under the finger-nails. Many teeth are carious and there is some pyorrhœa alveolaris. The body shows definite evidence of emaciation. The eyes are sunken; the cheek bones are prominent; the clavicles project; the supra- and infra-clavicular fossæ are very deep. The skin over the whole body is loose and pale. The posterior cervical, axillary, inguinal and epitrochlear lymph-glands on both sides are greatly enlarged, moderately firm, discrete and freely movable between the skin and the deeper parts. The external surface of the body otherwise shows nothing of interest.

The *peritoneal cavity* presents a smooth, glistening serous surface throughout. Here and there are some fibrous adhesions. The margin of the right lobe of the liver extends 3 cm. below the costal margin in the right mammary line. The margin of the left lobe of the liver extends 5 cm. below the tip of the xiphoid. All the organs occupy the normal position, except for a slight displacement due to the large retroperitoneal and other lymph-glands.

The left pleural cavity is empty and presents smooth and glistening surfaces. The right pleural cavity is obliterated by fibrous adhesions.

The *thymus*, although carefully searched for, could not be demonstrated.

The *pericardial cavity* contains the usual amount of clear, straw-colored fluid. Its serous surfaces are uninvolved.

Heart.—Presents nothing of interest. The left myocardium on tangential section is uniformly reddish brown. The coronary arteries contain a few atheromatous patches. The root of the

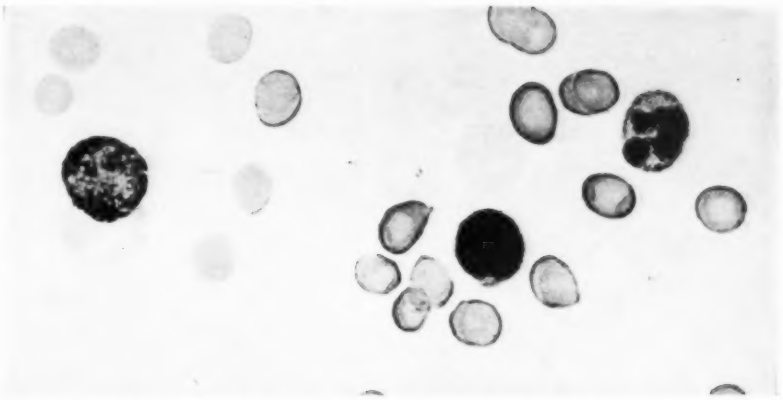

FIG. A. Blood of Case I (×1000). Showing 2 myeloblasts and 1 polymorphonuclear neutrophile.

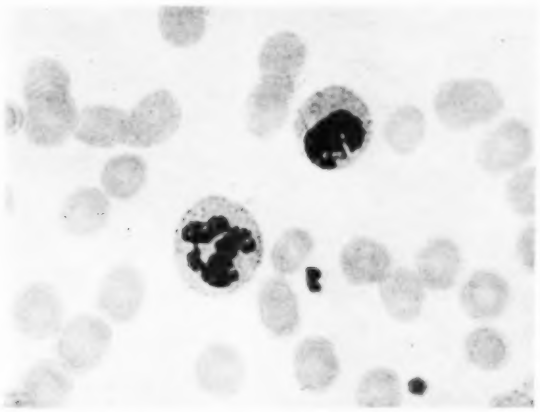

FIG. B. Blood of Case II (×1000). Showing young polymorphonuclear neutrophiles.

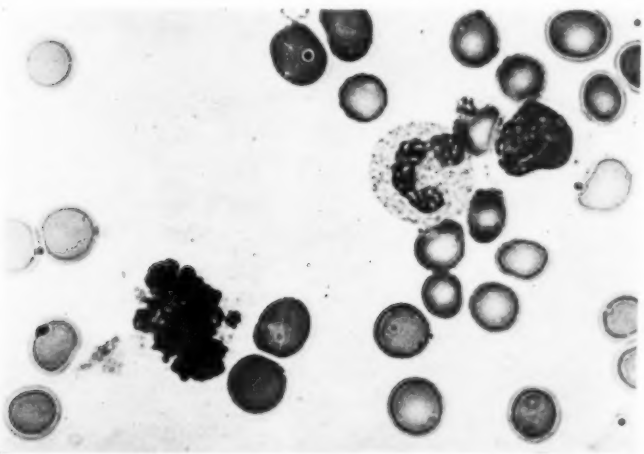

FIG. C. Blood of Case III (×1000). Showing lymphocyte, polymorphonuclear neutrophile and smudge.

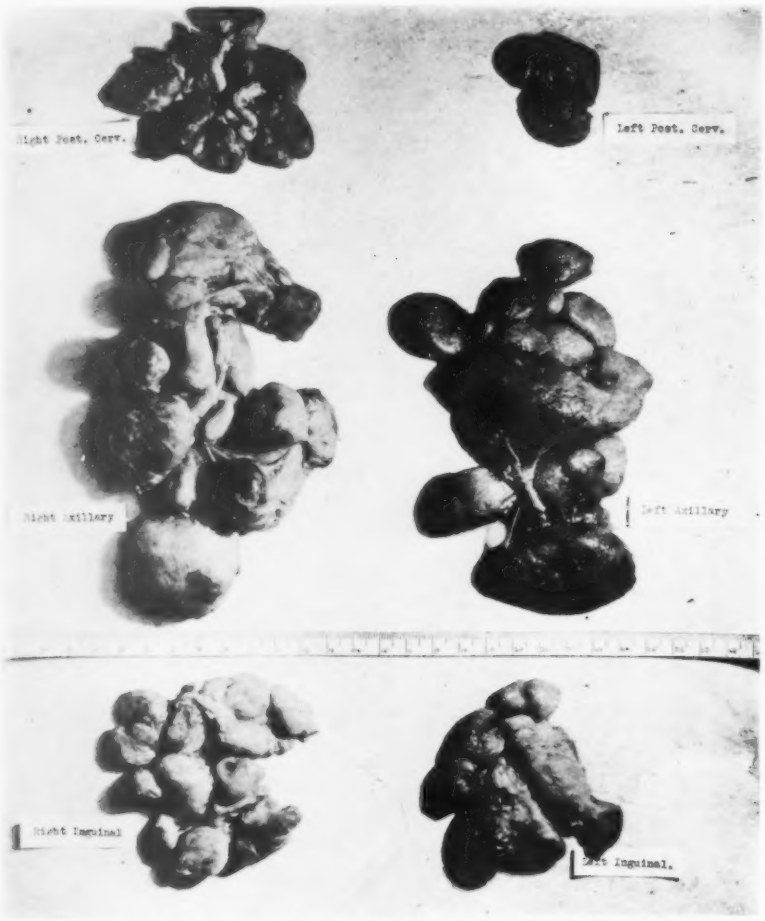

FIG. 1. Superficial lymph-glands. Note increase in size.

FIG. 3. (a) Retrothoracic lymph-glands. (b) Retroperitoneal lymph-glands. (c) Mesenteric lymph-glands. (d) A very large pancreatico-hepatic lymph-gland. (e) Pancreas. (f) Duodenum. (g) Mesentery. (h) Large vascular lymph-gland in region of the left adrenal and kidney.

FIG. 2. Superficial lymph-glands. Note the diffuse hyperplasia of the lymphocyte with absence of follicles. The capsule is shown in upper right hand corner.

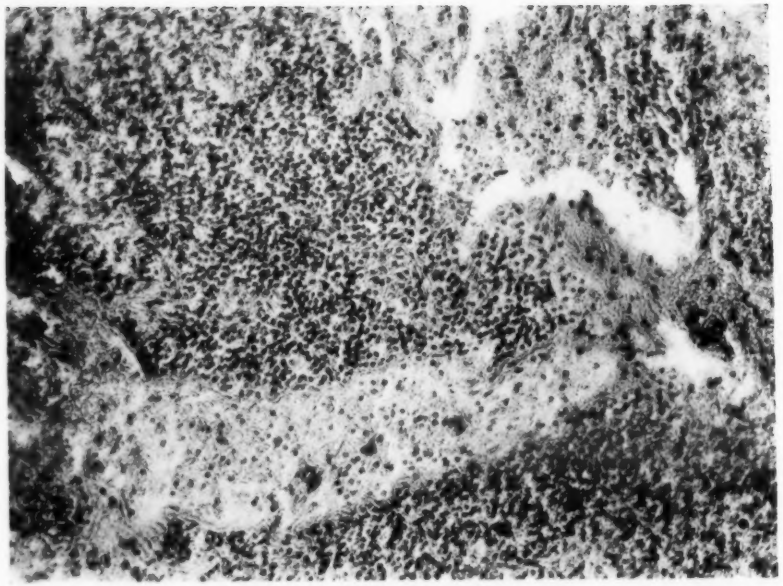

FIG. 4. Large lymph-gland in left kidney region. Note the very vascular, diffuse, lymphocytic hyperplasia with absence of follicles.

FIG. 7. Liver. Greatly enlarged. Note the characteristic periportal gray network.

FIG. 5. Spleen and right kidney. Note the increase in size of both organs and the characteristic gray granules of both surfaces of kidney.

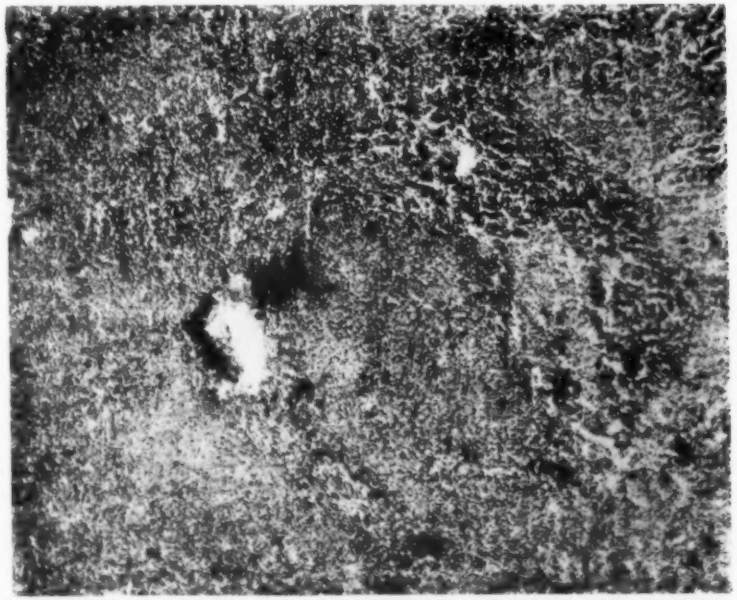

FIG. 6. Spleen. Note the hyperplastic Malpighian bodies.

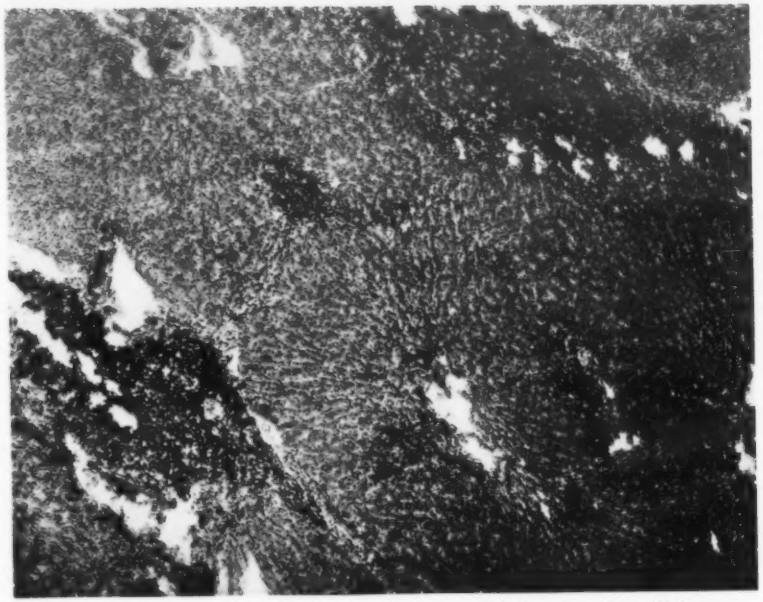

FIG. 8. Liver. Note the hyperplastic perilobular lymph follicles.

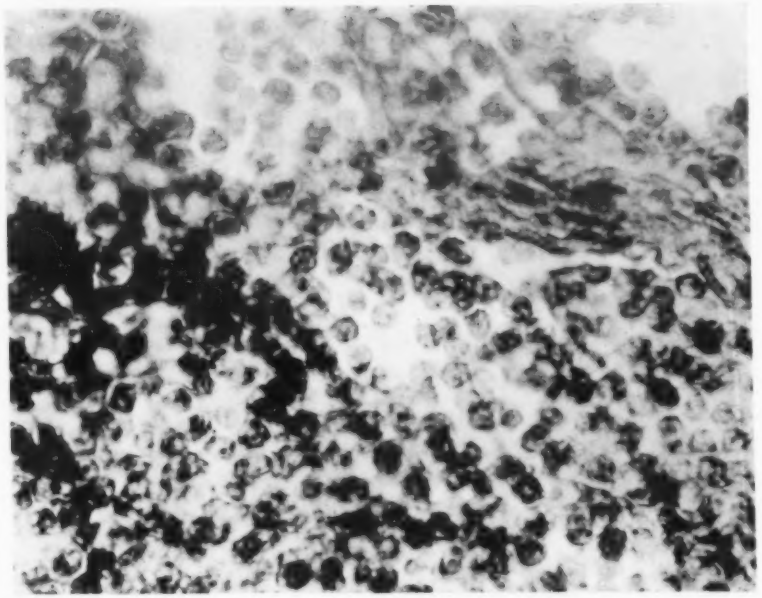

FIG. 9. Liver. High power of a perilobular lymph follicle, to show type of cell (lymphocyte).

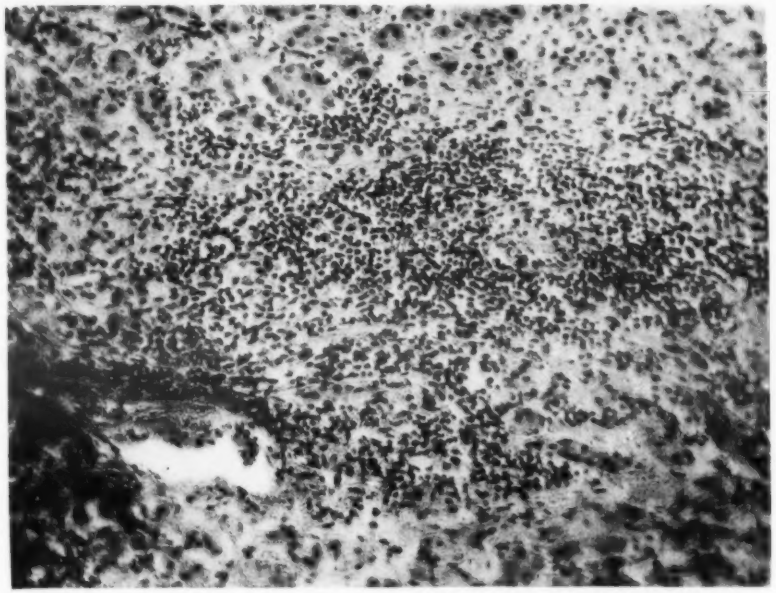

FIG. 10. Adrenal. Note the mass of lymphocytes in the medulla.

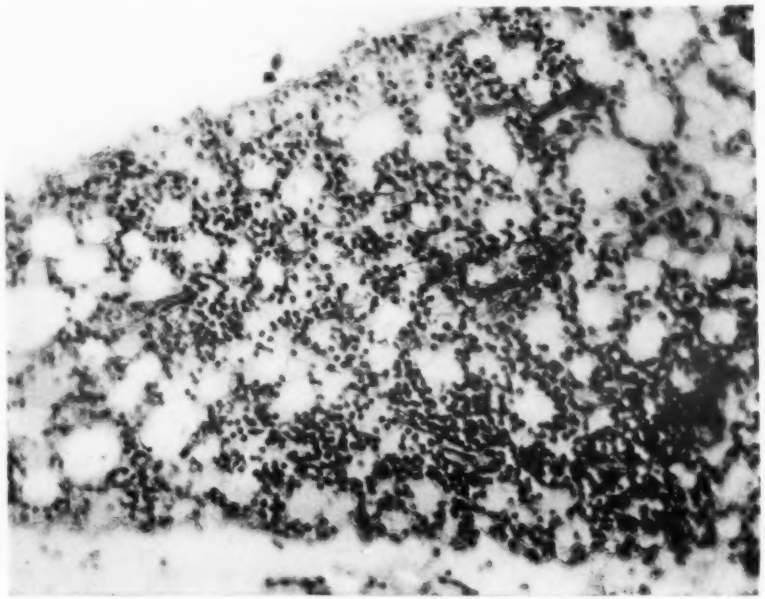

FIG. 11. Periadrenal fat. Note infiltration with lymphocytes.

pulmonary artery and aorta show here and there yellowish-white, opaque, slightly elevated patches.

Lungs.—Both lungs have practically the same appearance. They are large, pale, grayish pink and air-containing throughout, with large alveoli. On section, the surface is smooth, gray with unusually large air spaces. The bronchi, arteries, veins and the hilic lymph-glands present nothing of interest.

Spleen.—The *spleen* is greatly enlarged. It weighs 600 gm. and measures 18.0 x 13.0 x 5.5 cm. Its capsule is somewhat thicker than normal and of a slightly milky appearance. The spleen is practically normal in shape, except that its edges are more round. It is slightly soft. On section, the capsule and trabeculæ are prominent; the Malpighian bodies are larger than usual. The pulp is reddish brown and does not rise or recede from the cut edge.

Stomach.—The *stomach* is of normal size and shape, and when opened presents nothing of interest except a small, superficial ulcer, about 0.5 cm. in diameter near the pyloric end on the posterior wall. Near-by, there is a slightly elevated, oval, gray area of about the same size. The duodenum externally and on section presents nothing of interest. The bile and pancreatic ducts are patent.

Pancreas.—The *pancreas* is of normal size and shape. It was not weighed but it measures 23 cm. in length. It has the normal yellow color, normal lobulations and consistency. On section, it shows the usual structure.

Liver.—The *liver* is very large. It weighs 2480 gm. and measures 30 x 22 x 9 cm. It is practically of normal shape except that its margins are slightly rounded. Its consistency is about normal. The capsule is delicate. Beneath it may be seen the lobulation. The center of each lobule is yellowish brown and the periphery is gray, forming a distinct network over the surface of the organ. On section, this lobulation is very pronounced and answers to the same description. The *gall-bladder* presents nothing of interest.

Adrenals.—The right adrenal weighs 6 gm. It is very soft. On section, its capsule and cortex present nothing of interest, but the medulla is scarce in amount and the cortical portions are separated, due to softening of the medulla. Left adrenal (see below).

Kidneys.—The right kidney is relatively larger than normal. It weighs 200 gm. and measures 13.5 x 7.5 x 4.5 cm. It is of normal shape and consistency. Its capsule is delicate and strips readily, leaving a slightly yellowish, granular surface. On section, the cortex is unusually wide, averaging 12 mm. The striæ are very distinct. The glomeruli can readily be seen as tiny bright red pin-points. Parenchymatous striæ are broad and gray. The striæ of the pyramids are also prominent. The pelvis and ureter present nothing of interest. Left kidney (see below).

Pelvic Organs.—The rectum, bladder, prostate, seminal vesicles and vas deferens present nothing of interest.

Intestines.—The small intestine throughout presents nothing of interest, but the cæcum and all of the colon excepting the rectum show extensive ulceration, most marked in their upper half. The ulcers are long and narrow, extending around the gut. They involve the entire thickness of the mucous membrane, undermining it, but seem to stop at the inner muscle layer. They are clean and show no reaction. The process is most marked; hardly half a centimeter of normal intestine remains between any of the ulcers.

Testicles.—Both testicles and epididymes are normal.

Lymph-Glands.—The lymph-glands of the retrothoracic and retroperitoneal regions and those which lie between the pancreas and the liver and those at the root of the superior mesenteric artery are very large, soft, juicy and mottled. They are gray, with splotches of bright red. On section, they are either of this appearance or are uniformly gray. One lymph-gland just above the pancreas, between it and the liver, is very large. It measures 8.5 x 5.5 x 3.0 cm. The largest of the retroperitoneal lymph-glands measures 4.0 x 2.4 x 1.5 cm. The superficial lymph-glands, above mentioned, all present the same picture externally and on section. In addition to what has been said, they are uniformly gray in appearance both externally and on section. The axillary lymph-glands on both sides are the largest and most numerous. The largest on the right side measures 6.0 x 3.5 x 2.5 cm. The largest on the left side measures 5.0 x 3.5 x 2.5 cm. These superficial lymph-glands differ from the retroperitoneal and retrothoracic lymph-glands in that they seem to be less acutely involved. The left adrenal and kidney are buried in a red fluctuating mass.

After careful dissection of this mass, a normal appearing adrenal is exposed. The left ureter, which appeared normal externally, when opened, is traced into this mass of lymph-glands, and ends in a slight dilatation about 4 cm. long and 2 cm. wide. Along one side of the same is a zone, 2 cm. wide, of what appears to be renal tissue. This is all that can be demonstrated of the left kidney. The renal vein appears normal and can be traced to the inferior vena cava. The left renal artery at its origin from the aorta has a lumen of 0.2 cm., while that of the right renal artery is 0.6 cm. in diameter. The left artery has been cut across about 1 cm. from its origin. Its entry into the kidney pelvis cannot be demonstrated. (The above was considered to be a congenital atrophic kidney.)

Bone-marrow.—The bone-marrow, taken from the rib, appears grayish red and is moderate in amount.

Microscopic Notes.

Heart.—Sections show a small mass of lymphocytes between the muscle fibers.

Lungs.—Moderate emphysema.

Spleen.—The Malpighian bodies are very large, otherwise they and the rest of the section show nothing unusual.

Stomach.—Sections from the ulcer show that it has undermined the mucous membrane at its edge and has extended to the first muscle layer. The mucosa and submucosa contain small masses of lymphocytes.

Sections of the gray nodule near the ulcer show an extreme infiltration of all the layers of the stomach wall with closely packed lymphocytes.

Pancreas.—The pancreatic tissue itself is not implicated, but the peripancreatic fatty tissue is infiltrated with lymphocytes.

Liver.—Sections show practically every periportal space to contain a mass of lymphocytes. The lymphocytes are limited to these follicles.

Adrenals.—Sections of the right adrenal show an infiltration of lymphocytes in a localized area of the medulla. These are also present in the periadrenal fat tissue.

The left adrenal and its periadrenal fat tissue are not implicated.

Kidneys.—Sections of the right kidney show small masses of lymphocytes throughout the cortex, frequently near blood-vessels.

A section of the left kidney taken through the dilated terminal part of the ureter, obviously the pelvis, and the zone, a few millimeters wide, of renal tissue adjoining it, shows the following picture: A wide zone of fibrous tissue with small masses of lymphoid cells, bordered on one side by mucous membrane with several layers of imperfect columnar epithelium. Just below this surface are occasional gland-like structures, also lined with several layers of columnar epithelium. This part of the section is rich in lymphoid cells. In other parts of the section are structures which appear to be greatly dilated renal tubules with cuboidal epithelium.

Prostate.—Sections contain extensive accumulations of lymphocytes between the muscle and fibrous tissue.

Intestines.—Sections from the small intestines show nothing abnormal. Sections of the large intestine taken through ulcers show the same to involve and undermine the mucous membrane, extending to the inner circular layer of muscle. The tissue at

the margin of the ulcer is necrotic and infiltrated with polymorphonuclear cells, red blood-cells, and in some sections with fibrin. The near-by blood-vessels are congested. A fibrino-purulent membrane covers the bases of some of the ulcers.

Lymph-Glands.—Sections from the following groups of glands were studied: bifurcation of the trachea, the right and left posterior cervicals, the right and left axillaries, the right and left inguinals, mesenteric, pancreatic-hepatic, retroperitoneal.

All these different glands presented the same histological picture. The normal histological structure into lymph follicles, medullar strands of lymph cells, lymph sinuses, etc., has been entirely replaced by a diffuse, closely packed mass of lymphocytes, uniform in appearance everywhere inside the capsule. The capsule in places contains small masses of lymphocytes. The latter are also in large number out in the periglandular fat tissue.

The large, red, juicy mass which pressed upon the atrophic left kidney has the same structure as the lymph-glands above except that it is more vascular.

Bone-Marrow.—Sections of marrow from the ribs show entire absence of fat. The lymphocyte is by far the predominating cell.

The clinical diagnosis was "chronic lymphatic leukæmia" (aleucocythæmic at first). This was borne out by the pathological findings. The case is clearly an instance of what Naegeli would call "Aleukæmic Lymphadenosis." He recognizes six types of this disease, but the one reported here belongs clearly to the most common and easily recognized group, the group with generalized lymphatic hyperplasia, frequently with qualitative blood changes.

An interesting feature of the case is the effect of the X-ray and the acute infections upon the blood-picture. After two X-ray treatments, without other apparent cause, the white cell count rose from 7720 to 12,880; the polymorphonuclears rose from 37.6% to 59.0%, and the lymphocytes dropped from 50% to 29%. The absolute number of polymorphonuclears was greatly increased; the absolute number of lymphocytes was almost exactly stationary. At the onset of the pulmonary infection there was a definite increase in the total number of lymphocytes and a very slight polymorphonuclear increase. The dysentery was associated with a typical blood-picture of lymphatic leukæmia. During this infection the total number of lymphocytes was 17,503 per c. mm., and the polymorphonuclears numbered 12,443 per c. mm.

SUMMARY.

1. "Aleucocythæmic Leukæmia" seems to be a somewhat more satisfactory term to apply to those cases of leukæmia which show no increase of the total white blood-cell count than the commoner expressions, such as, aleukæmic leukæmia, aleukæmia, pseudoleukæmia, etc.

2. Fourteen of a total number of 105 cases of leukæmia on record at The Johns Hopkins Hospital were without leucocytosis at some time while under observation.

3. Three cases of aleucocythæmic leukæmia are reported in detail. One is a case of acute myeloblastic leukæmia, which went to a fatal termination, probably without ever having leucocytosis. The second is one of possible chloroma. It occurred in an elderly patient and was characterized by a chronic course, but the physical signs and the anatomical appearances in an excised subcutaneous nodule were very suggestive of chloroma. The third case is one of chronic lymphatic leukæmia, with a high mononuclear percentage, the blood picture of which was changed from that of an aleucocythæmic to that of a typical lymphatic leukæmia during an acute bronchitis and an acute bacillary dysentery.

OBSERVATIONS BEARING ON THE POSSIBILITY OF DEVELOPING AN EXPERIMENTAL CHEMOTHERAPY OF TUBERCULOSIS.*

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It is a matter of record that, directly after his discovery of the tubercle bacillus, Koch devoted a great deal of attention to efforts to cure experimental tuberculosis in animals. Cornet,[1] then an associate of Koch, records the negative results of experiments with a certain number of drugs and chemicals in this endeavor.

The experiments made in this earliest work on the experimental therapy of tuberculosis naturally rested in large part on an empirical basis. The hope that an effective method of treatment could be arrived at in this way was based on no precedent. The materials chosen were naturally those that had some reputation as active agents in the treatment of tuberculous lesion in human beings.

It was a matter of course that a mind as logical as Koch's should have demanded the development of some more scientific basis for further experimentation. He proceeded on the tentative assumption that, if substances could be found with the capacity to check the growth of the tubercle bacillus in the culture flask, there might be those among them which would likewise restrain the proliferation of the parasite in the animal body. He accordingly carried out experiments with a large number of substances to determine their capacity to inhibit the growth of cultures. These experiments were not reported in any detail, either as to the precise methods employed or as to the quantitative aspects of the results attained. Koch[2] states that the following substances were especially active *in vitro:* "A number of ethereal oils, among aromatic compounds β naphthylamin, para-toluidin, xylidin; some so-called tar colors, namely fuchsin, gentian violet, methylen blue,

* Read before the Laennec Society, at The Johns Hopkins Hospital, March 27, 1916.

chinolin yellow, anilin yellow, auramin; among the metals, mercury in vapor form, silver and gold compounds. Gold-cyanogen compounds are especially striking in their surpassing activity over all other substances." Further: "All of these substances remained completely inactive when tested on the tuberculous animal."

In the course of these experiments it was found that a certain substance which could be extracted from the growing cultures was capable of profoundly influencing the progress of experimental tuberculous disease in guinea-pigs when administered to them during its course. In the first experiments the influence seemed to be of a curative nature and the substance, known at first as "Koch's Lymph," later as "tuberculin," was introduced into medical practice. What may be called the physiological activity of tuberculin is now a matter of common knowledge. Whether this activity can be so applied that the substance can be considered a useful therapeutic agent has been from the very beginning a matter of violent and almost fruitless controversy. As I have already pointed out elsewhere,[2] any evidence which may be in favor of the usefulness of tuberculin in practical therapy is derived from clinical observation. This question is raised, not because it directly concerns the matter in hand, but because it is apparent that, as a matter of history, the discovery of tuberculin, the violent controversy that it excited and the brilliant discoveries in the field of serum therapy which followed so soon after, caused this early experimentation with well-defined chemical substances to be abandoned and for the time forgotten.

Then followed a period of 15 years, during which no observations of any interest in this field were recorded. Those interested in the disinfectant activity of various chemicals frequently included the tubercle bacillus in their lists of micro-organisms tested. The methods employed were not uniform and the chemicals were selected according to no general plan. As the chief result of present interest in the scattered work of this period, it has come to be recognized that the tubercle bacillus, as contrasted with other common pathogenic bacteria, is difficult to kill with chemical disinfectants. In this period there should be noted the paper of Boer[4] on certain aspects of the activity of disinfectants. Working with a number of non-related substances, he found that there were certain differences in the intensity of the action of various substances against cultures of non-related species of bacteria.

This concept was developed further and practically applied to the differential cultivation of more closely related species by Loeffler, Conradi, and others. It was found that various anilin dyes, malachite green in the first instance, cresyl violet, crystal violet and basic fuchsin in later cases, markedly check the growth of *B. coli* or various troublesome micrococci in concentrations which do not inhibit the growth of *B. typhosus*.

To substances showing this type of differential activity Bechold and Ehrlich[5] applied the term partially-specific (halb-specifische) disinfectants in contradistinction to the more highly specific bacteriolysins of the blood serum of immunized animals. These authors applied the highly complicated methods of synthetic organic chemistry to the development of a series of closely related chemical compounds whose disinfectant activity they then studied from this point of view. Their studies revealed the most striking examples of this partially specific disinfectant action. For instance, tribromnaphthol was found to possess a very strong disinfectant action against staphylococci, streptococci and diphtheria bacilli, very little against *B. pyocyaneus* and none at all against the tubercle bacillus. Monochlornaphthol is more active against staphylococci than cresol, but far less active than tribromnaphthol. Against the pyocyaneus and the tubercle bacillus, on the contrary, monochlornaphthol is very active.

The early efforts of Ehrlich to develop chemotherapeutic agents for use in experimental trypanosomiases were much influenced by the thought that test-tube study of the disinfectant action of substances against the parasite could be used as a clue to the chemicals which it would be profitable to study subsequently in animal experiments. The expectation, in these instances, proved without foundation and in fact the substances more active *in vivo* often had very little activity in the test-tube. It would probably be short-sighted to conclude from this experience in a very special field that test-tube results could never be useful as a guide. And in fact, the recent observations (after the fact, so to speak) of Schiemann[6] show that salvarsan, inactive in the test-tube against protozoa, but very active in the body, is active in the partially specific sense against certain bacteria, both in the animal body and in the test-tube.

The hope, so evidently entertained by Koch, that it would be possible to develop in a rational way specific chemical agents to cure particular diseases (tuberculosis first of all in his mind), fulfilled in the most spectacular way by Ehrlich at a time when it had been abandoned as a moving conception in the minds of most workers, has again become a dominating factor in many laboratories where tuberculosis is a subject of study. The general considerations which must be taken into account when the principles developed by Ehrlich are applied to the study of tuberculosis have been well stated and at length by Wells[7] and his associates, and need not be further discussed here. We reiterate, for the sake of emphasis only, that the methods of handling tuberculosis experimentally and the conception that it might be possible by systematic search to find a rational treatment we owe to Koch. The model for such a search, the realization of the vast labor by a highly complex organization which must be contemplated as probably essential to achievement, and finally, the demonstration that for one radically different but equally tenacious disease (syphilis) success along these lines is possible, we owe to Ehrlich.

It may be profitable to consider briefly in more detail what is involved if we are to try, with hope of success, to apply the principles of Ehrlich to tuberculosis research. In the first place, Ehrlich's success was in no small measure due to the fact that he had to deal with experimental diseases whose course was rapid and whose limitations were very precise. From the time of infection to certain death in the untreated animal was in his typical case three or four days, and the exact condition of the animal could be determined at any moment by a simple examination of the blood. In our case we have no

such favorable basis for experimentation. In laboratory animals infected with properly selected cultures, death is certain, but the length of life is very uncertain except after most overwhelming doses, and I know of no experiment which can be terminated in less than a month. Many require much longer before an interpretation is possible.

Before this Society, four years ago, I reported observations on experimental tuberculosis of the cornea made with the cooperation of Dr. Montgomery,[8] which we hoped would give a good basis for therapeutic tests. This lesion is useful for the study of certain features of the disease but fails in other very important particulars. Much further work is needed to develop conditions under which the generalized disease or local lesions will run a precise and invariable course. It is not to be expected that high speed will be attained, but the shorter the course the more useful will be such a reaction as a basis for work.

On the other hand, tuberculosis is a field of study offering certain distinct advantages. The bacteria are demonstrated in the tissues with comparative ease and certainty; in the tissues they cause a very distinct local lesion; and the distribution of certain chemicals to this diseased tissue can be very precisely followed.

This last factor, the distribution of drugs to the tissues, has been the starting-point for a number of recent researches, and for some premature efforts in the treatment of the human disease. Our own recent work has been very greatly influenced by the observation that certain anilin dyes, when injected into the living tuberculous animal, become concentrated to a considerable extent in the diseased tissues. On the occasion of a visit to Baltimore four years ago, to attend a meeting of the Society, I was shown some very beautiful preparations by Dr. Winternitz, preparations made in a study of the origin of the cells taking part in the reaction of the earliest hours after an infection of the animal with tubercle bacilli, and since carefully described by Bowman, Winternitz and Evans.[9] My interest was aroused in the possibility of making a wider application of the so-called vital stains, and I soon found by experiment that the fibrocaseous tubercle took up these stains in a characteristic way. The results of these early experiments were recorded and summarized in the following terms:[10]

> The first of these experiments shows again the selective action of Isaminblau for the large mononuclear phagocytic cell as pointed out by Goldman. These cells are found abundantly in the peripheral portions of fibroid tubercles.
>
> The second experiment is of great interest, showing, as it does conclusively, that extraneous chemical substances of proper constitution may within a few days penetrate to the caseous center of a tuberculous mass and become concentrated there in greater degree than in the normal surrounding tissues. The particular substance used in this experiment, Trypan-rot, may probably be without effect on the lesion itself, but the result should be a great stimulus to future work in a similar direction.

These experiments have seemed to us of the utmost importance as a basis for further experimental work of a co-ordinated chemical and biological nature. The opinion had been quite generally expressed that, since the tuberculous tissue was without an internal blood supply, it could be reached only with difficulty, if at all, by medicinal agents which might be made to circulate in the blood stream. Such an opinion, if of decisive weight, would make it appear to be an unreasonable waste of time to experiment to any great extent with the idea of developing general medicines that might be hoped to influence the local tuberculous process. The actual result, on the contrary, rendered such experimentation reasonable and, as it seemed to us, eminently desirable.

Before dealing in greater detail with our subsequent work on this subject, I wish to refer briefly to certain observations of others. Independent observations by De Witt[11] in this country and by von Linden[12] in Germany have shown that when methylene blue, or any one of several of its modifications, is introduced into the living diseased animal, the leuko-base of the dye is to be found in the caseous portions of the tubercle. Since methylene blue strongly restrains the growth of the tubercle bacillus outside the body (von Linden claims that the leuko-base is more strongly germicidal for the tubercle bacillus than the dye itself), and since, moreover, von Linden asserts that the tubercle bacillus is stained in the lesions, it would seem that nearly all the desirable qualities that could be postulated for the object of our search are possessed by this dye. Suffice for the moment to say that the work of von Linden is considerably offset by criticisms offered by her colleagues and former associates, and that De Witt's results are not in accord with it in many important particulars. For the past four years the work of Dr. De Witt and Dr. H. J. Cooper in the laboratories of the Sprague Memorial Institute, Chicago, under the direction of Dr. H. G. Wells, has followed the same general course as the work in the laboratories of the Phipps Institute. As we have used quite different materials, the two series of researches are to be considered as complementary.

Returning now to the progress of our own experiments, I would call your attention to the obvious, and say that the further development of such a subject as this is dependent on the pursuit of both chemical and biological studies in a carefully co-ordinated way. I have been fortunate in having as an associate Mr. R. B. Krauss, and throughout the rest of the paper, whenever points involving chemical manipulation are referred to, the work is to be credited to him.

The first concrete problem outlined on the basis of the above experiments was to take the dye "Trypan-rot," which had been used in the more striking of the experiments above commented on, and try by chemical manipulation to form from it or with it a substance having physiologic activity while preserving the qualities which enabled the dye to penetrate the tubercle.

Mr. Krauss undertook to make as many modifications of trypan red as he could, following certain general lines.

1. The staining qualities of the substance were to be at least in part preserved.

2. The preference was to be given to substances containing iodine, phenolic substances, or certain other constituents.

These specifications were drawn up on very general grounds, some of which may be stated as follows: Iodine was selected

because of the long-standing belief among medical men that iodine had some influence unfavorable to the progress of tuberculosis when applied locally either as an element or as iodoform; carbolic acid, guiacol and other phenolic substances were known to be relatively active disinfectants against the tubercle bacillus, and some of them also enjoyed a reputation as medicines for this disease. The staining qualities were to be preserved as far as possible as a guide to the localization in the course of the subsequent animal experimentation.

The chemical work was successful. In the course of a year and a half about 75 compounds were secured on the plan outlined. The chemical manipulations and results have been published by Krauss.[12] These preparations were used in a preliminary way in animal experiments, and some interesting observations were made. In general it was indicated that none of the substances exerted any curative influence on experimental tuberculosis. Some of them seemed, however, to have a definite influence on the vigor and rate of the formation of blood vessels and connective tissue in and around the tuberculous process; the tests being made on the cornea of the rabbit.

The plan had been to prepare enough of each substance for a moderate amount of preliminary experimentation and then to make some more of those which seemed useful for further work. About the time the preliminary study of these compounds was completed, the war began and necessitated a change of plan. We had been purchasing trypan red from abroad and a further regular supply was unobtainable. What was on hand and the occasional lots since secured we have used in a study of the composition of the substance with view to its manufacture.

Trypan red was first made for Ehrlich and was assigned a definite chemical formula by him, presumably based on the method of manufacture. On the basis of this formula the manufacture of the substance should be relatively easy, but we have not succeeded in carrying it out. On the contrary, we have been able to show that the trypan red of the German market does not agree with its constitution as given by Ehrlich. Only by continued analyses can we hope to learn how to make the substance. Under the present circumstances the work we have done in this particular field cannot be used to advance the subject until we are able to repeat our experiments with certain of the preparations and do it in such a way that they may be susceptible of repetition by others. I have reason to believe that these difficulties will be overcome in due time. We have meanwhile been searching for some other substance which might have the essential properties of trypan red and which at the same time could be made by us.

Following our observation that the tuberculous tissue in the living animal was easily penetrated by trypan red, many other dyes of the same general class, chemically speaking, were tested for their reaction in this particular. A considerable number were found which could become concentrated in the diseased tissue to a greater or less extent. Many of these had never been accurately described from a chemical point of view; others presented difficulties in manufacture beyond our means. After much consideration, a dye known to the trade as Niagara blue 2B (Benzidin + ? H. Acid) was chosen as the starting-point of a second attempt to construct a series of iodine and phenol compounds. Owing to the state of the chemical trade it has been necessary for us to build up this substance from the raw products. This has now been accomplished on a scale adequate for the purposes of our work, and we have recently had available a small series of finished compounds for further biological study. It is unlikely that these substances will replace those made with trypan red, but they are fully as likely to be instructive, and we now have the assurance of a solid foundation for the work.

Covering about the same period of time as these studies on the relation of the vital stains to the diseased tissue, and in the hope of acquiring information which should in some measure guide that work, we have been studying the disinfectant action of various substances for the tubercle bacillus. We have hoped to discover more substances having the partially specific action discussed in the earlier paragraphs of this paper. Much time has been spent over methods. The procedure by which the results here reported were obtained was to determine the least concentration of the substance in glycerin-bouillon which would definitely inhibit the growth of the tubercle bacillus. For comparison, from the side of the bacterial species we have used so far chiefly the typhoid bacillus, determining in the same way the concentration of the substance required to prevent its growth in the same medium.

Because of the relation to the work outlined in considering the subject of the vital stains, we have so far paid particular attention to anilin dyes. We have also considered the more common disinfectants and certain substances which are used in the building up of dyes.

Certain rather striking observations have been made, which may be briefly recorded here. We hope to publish shortly a report covering the examination of several hundred substances by this method.

I. PHENOL (CARBOLIC ACID).

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/800	No growth	No growth
1/2000	Good growth	No growth
1/4000		Good growth

II. RESORCIN.

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/1000	No growth	
1/2000	Good growth	No growth
1/4000	Full growth	Mod. growth
1/20,000		Good growth

III. No. 158—BROWN DYE MADE BY COUPLING BENZIDIN AND RESORCIN.

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/200	Mod. growth	
1/400	Full growth	
1/20,000		Very slight
1/40,000		Mod. growth
1/100,000		Mod. to full growth

IV. ACRIDIN ORANGE. (DYE WITH ACRIDIN AS A BASE).

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/2000	No growth	
1/4000	Full growth	
1/100,000		Slight growth
1/200,000		Mod. growth
1/400,000		Full growth

V. Heliotrope (Kalle & Co.) (a Dye Related to Safranin).

Concentration.	Typhoid Bacillus.	Tubercle Bacillus.
1/1000	No growth	
1/2000	Very slight	
1/4000	Mod. growth	
1/10,000	Full growth	
1/400,000		No growth
1/1 million		Mod. growth
1/2 million		Mod. growth
1/4 million		Full growth

Taking from these tables the concentrations at which the effect on growth appears to be equal, and considering the susceptibility to the action on the part of the typhoid bacillus as unity, the following figures for the susceptibility of the tubercle bacillus are obtained:

Phenol. Typhoid 1/800 = T. B. 1/2000 or susceptibility of T. B. = 2½.

Resorcin. Typhoid 1/4000 = T. B. 1/100,000 or susceptibility of T. B. = 25.

No. 158. Typhoid 1/400 = T. B. 1/100,000 or susceptibility of T. B. = 250.

Acridin Orange. Typhoid 1/4000 = T. B. 1/400,000 or susceptibility of T. B. = 100.

Heliotrope. Typhoid 1/1000=T. B. 1/400,000 or susceptibility of T. B. = 400.

These striking instances serve to illustrate the simplest phase of the problem. The data so far collected for consideration make certain more general statements possible.

(a) Of the anilin dyes, this partially specific activity is manifested quite generally by those related to safranin and to acridin. It is shown in greater or less degree by many of the azo-dyes made with benzidin as the basic constituent. On the whole the number of substances showing this property is large rather than small.

(b) Although in the studies previously made with other bacteria, the concentration required to inhibit the growth of the culture is roughly proportional to the higher concentration required to kill the microorganism in a short period of time, with the tubercle bacillus this is not the case. So far we have discovered no substance by which the tubercle bacillus is killed more readily than is the typhoid bacillus, and while we have used the term "partially specific disinfectants" in recognition of the work of others along similar lines, it would be more nearly correct to speak of partially specific inhibitors of growth.

(c) The ability to inhibit the growth of the tubercle bacillus in cultures is not dependent on high disinfectant activity in general, and is an attribute of a number of substances which are relatively non-toxic for higher animals.

In conclusion, I feel that the results described in the preceding pages form a substantial foundation for future work. With the localization of the dyes in the centers of the masses of tuberculous tissues and in certain cells in the peripheral portions of the same, the problem of distributing extraneous chemical substances to the diseased tissues was solved in its grosser aspects. It is equally clear that relatively non-toxic substances may be very active in restraining the growth of the tubercle bacillus outside the body. It may be predicted with a fair degree of assurance that there will soon be at hand a number of substances which can be concentrated in the diseased tissue, and which will at the same time possess in considerable degree the ability to restrain the growth of the tubercle bacillus in cultures. This we are disposed to think will mark a distinct step in advance toward the solution of the abstract problems involved in the development of a specific therapy for tuberculosis as contrasted with our position of five years ago.

Will it mark a long step toward the practical treatment of tuberculosis? It is unlikely. There is still no scientific observation to guide us further toward a substance having these qualities and also capable of coming into effective contact with the tubercle bacillus in the body tissues and fluids, considered minutely.

It should also be fully recognized by everyone concerned that the practical problem of treating tuberculosis may be a far more difficult thing to accomplish than its laboratory prototype. Certainly it will be a most unfortunate thing for the progress of tuberculosis research if every substance showing interesting properties in the laboratory is immediately rushed to the clinic regardless of consequences. In this situation, patience is to be taken more than usually as an evidence of virtue.

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DISCUSSION.

Dr. Ford: I do not feel that I am in a position to say very much about work of this character, which so manifestly has consumed many hours of energy, and such extended intellectual effort. Dr. Lewis's paper is a great surprise to me in some respects. I do not think that *a priori* any of us would have expected the tubercle

bacillus to be more sensitive to disinfectants than are other organisms. This calls to my mind the controversies which existed for some time after the bacillus was discovered. You may remember that the granular bodies that appear in the bacilli were first interpreted as spores. The proof that they are not spores rests upon their low thermal death point and upon the fact that the tubercle bacillus is not so resistant to disinfection as are organisms that produce spores. There are a number of phenomena suggesting that the tubercle bacillus is not destroyed at a temperature below 75 C. Other indications are that the thermal death point is 60 C., as for the ordinary non-sporulating bacteria. The matter was settled by Theobald Smith in experiments in which he showed that there had been certain fundamental errors in the observations of previous workers, and that if you took the tubercle bacillus and determined its thermal death-point with due regard to the fact that it is necessary to disinfect all parts of the tube, if you avoid all errors, the tubercle bacillus is found not to resist any greater degree of temperature than organisms like the typhoid or the color bacillus.

I do not think that anyone imagined that the tubercle bacillus was going to prove more sensitive to the action of drugs than are ordinary bacteria. In this connection Prof. Phelps of the Public Health Service demonstrated that, in ordinary disinfection, there are always some organisms that survive for long periods of time, and he regards disinfectants as acting according to chemical laws.

I do not recall whether Professor Phelps's work has even been confirmed or not. There are, however, some interesting things which have some relation to it and which tend to confirm it. If, for instance, you attempt to determine the action of heat upon milk and estimate the number of bacteria in milk and try to find the point at which all bacteria are destroyed, you find yourself beset with countless difficulties. You cannot easily find the point at which all bacteria are destroyed, and if you plot out your results, you get a curve like the one obtained by Professor Phelps with the disinfectants. In the same way Sedgwick and Winslow found that the destruction of bacteria in ice followed the same sort of curve. I do not know that this is any explanation of the points that Dr. Lewis has suggested, but it is analogous.

In connection with what Dr. Lewis said about the action of dyes immediately after heating, it is interesting to know that one sometimes gets similar reactions in saponin. If you heat your solution of saponin to determine the thermal death-point, you do not always find it, but the tubes which have been heated seem to be much more hæmolytic than the saponin was before it was heated.

Finally, it is very interesting to recall the influence of Ehrlich upon this work. After all, most of our studies in regard to disinfection followed along a certain level up to the time of Ehrlich's work, but since then we have had an entirely new series of observations which are extremely important.

NOTES ON NEW BOOKS.

Hygiene and Sanitation. By SENECA EGBERT, A. M., M. D. (*Philadelphia: Lea & Febiger, 1916.*)

The sixth edition of Egbert's Hygiene and Sanitation, published by Lea & Febiger, is a compact and comprehensive manual of about 500 pages, which deals exclusively with subjects bearing upon public health questions. In this edition a successful attempt has been made by the author to bring the subject matter up to date, although some of the older theories and earlier views are retained.

The addition of a new chapter upon Industrial Hygiene and Occupational Diseases is a clear response to the growing public appreciation of the importance of social hygiene.

The subject matter of the manual is divided into 16 chapters, each one of which takes up a subject of vital importance to public health. The subject matter is clearly presented without any unnecessary complications from the use of technical or medical terms. It should prove of great value to the general practitioner of medicine who has little time to go deeply into the subject of hygiene and who will find in this book concise and exact descriptions of the most important topics in sanitary science. It should also prove valuable to the medical student, since it will afford him the requisite information in a brief space, with accurate references to more extensive treatises on the subject. Finally, the non-medical man, the sanitary and the scientific student, should find the publication extremely helpful because of the simplicity of presentation. W. W. F.

The Criminal Imbecile. By HENRY HERBERT GODDARD, M. D. (*New York: The Macmillan Company, 1915.*)

The aim of Dr. Goddard's book—to "help the lawyer make a more successful defense of the imbecile criminal, the judge to dispense justice to this much misunderstood class of high-grade imbeciles, and society in general to realize its responsibility for the mental defective"—is certainly a laudable one, and to this end the material is presented in an interesting, simple, and logical manner, and the discussion is pertinent.

Details are given of three murders committed by as many high-grade imbeciles, and following this are chapters on "The Criminal Imbecile," "Responsibility," and "Punishment." In conclusion we find appendices full of bewildering legal hypothetical questions and lawyers' charges, which are eloquent proofs of the need of revision of the existing laws that deal with the mentally abnormal criminal.

The three murders were committed by youths belonging to a class that ordinarily floats along undetected in society, but which on skilled examination proves to be high-grade imbecile in its mentality and adaptation. The cases are unusual because of the use in court of the Binet-Simon tests as legal evidence of the prisoner's inferior mentality.

In the chapter on "Responsibility," Dr. Goddard feels that children or defectives with a mentality of 12 years or under do not know much about right and wrong, and that the imbecile knows the nature but not the quality of his act.

In regard to punishment the author sanctions life commitment to an institution for defectives or even a state prison. In connection with this point the broader and more fundamental problem of preventing imbeciles from becoming criminals is taken up, and emphasis is laid on the importance of early recognition and supervision of defective states. The chapter concludes with a plea for the study of defective school children with especial reference to reducing the birth-rate of these individuals and preventing further propagation—the root of the whole problem.

The book can well be recommended to physicians as well as to lawyers and laymen, and Dr. Goddard is to be commended for the production of such a timely addition to the mental hygiene movement. R. W. H.

Human Physiology. By PROFESSOR LUIGI LUCIANI. Translated by FRANCES A. WELBY. Price $5.00. (*London: Macmillan & Co., Limited, 1911.*)

Luciani's Physiology stands midway between the text-book designed primarily for the use of beginning students and the reference book intended for those advanced in the subject. English readers will appreciate the charm of a new point of view in dealing with the problems of physiology—that of the Italian school, of which the author is an eminent representative. The book,

furthermore, brings to light a considerable amount of Italian work, which has suffered more or less oblivion because American readers, at least, have been prone to confine themselves to French and German sources. Perhaps the greatest charm, however, lies in the historical treatment of the subjects under discussion; here the author seems not only to have found delight himself, but to have been able to convey to the reader an equal pleasure in the slow but patient unfolding of the various problems through scientific effort.

As may be inferred from the fact that each volume contains over 500 pages, the book treats of the subject matter in considerable detail; nevertheless, it has the advantage over most modern texts of this size compiled by multiple authorship that the style and point of view are throughout that of a single mind. None but a physiologist of the old school versed in all the branches of his subject could make such a contribution. Those of us who have felt the pressure of specialization may well pause to appreciate and admire a work of this nature.

Luciani is a confirmed neo-vitalist. Long before his text-book was written we may infer that he despaired of a solution of the phenomena of life according to the laws of chemistry and physics. Since, however, these offer our sole line of approach, it seems unfortunate to belittle the efficacy of our resources; the younger worker particularly, whose dreams sustain a determined purpose and in whom failure is still an inspiration, will rebel against this point of view. However true it may be that our instruments break and fail us of accomplishment, yet it does not necessarily follow that instrumentation is wholly impossible. Vitalism to the young man is an admission of failure, and as such is incompatible with the spirit of youth. Indeed, too many problems in science have been lifted out of the shadow of vitalism and advanced toward simplification to allow a final judgment. That the phenomena with which physiology concerns itself in time break the will to solve them with the means at hand is readily apparent, but in the matter of lymph-formation, for instance, it seems to the writer that the author far overstresses the significance of vital processes. Yet, however much we may distrust the neo-vitalistic conception of life, it is very proper that we should beware of the satisfaction of words and phrases—and this Luciani makes clear and imperative.

The author has sought successfully to place at the disposal of the reader many of the methods, operative, chemical and technical, which have advanced physiological thought, by detailed description of the procedures. Although these descriptions are not intended to supplant the assistance to be had in modern handbooks, they serve the useful teaching purpose of visualizing the method at hand.

Available sources of detailed information as to these methods and the chief contributions in literature are grouped at the end of the several chapters under the several subjects discussed. To this list, the editors of the English edition, Dr. Camis and Dr. Holmes, have added a selected list of English-written papers, which serves the double purpose of extending the field of available literature and of bringing the subjects down to a later date. The latter is a point of no small importance, in view of the present-day rapid extension of the science, and bears upon the one fundamental criticism of a book of this kind. Below, in referring particularly to the several volumes, the approximate date to which the literature has been followed will be stated. The fact that books, and especially text-books, serve their purpose and disappear is well apparent to everyone. It follows, therefore, that for practical application Luciani's text-book presented in English has necessarily depreciated in value. Nevertheless, the work of a master mind in any subject does not suffer greatly by the passage of time, provided the passage of time is appreciated by the reader. The beginning student should meet a subject brought fully up to date. The more mature student, however, can benefit from the older text, and to him the book under review will have a lasting value.

The English translation is to appear in five volumes, three of which are at hand. The first two of these follow the third, while the last three follow the fourth Italian edition.

The first volume deals with the circulation and respiration. It opens with an introduction and three introductory chapters dealing with the fundamental aspect of the biological problem, the purpose of which is to orient the reader, in preparation for the specific discussion and treatment which is to follow. Here we meet the first note of neo-vitalism which permeates the entire text. The subsequent chapters are notable for their wealth of illustration in the reproduction of graphic records, apparatus, diagrams and histological preparations, many of the latter being in colored plates. One is impressed by the insistence of the author in ascribing the discovery of the general circulation of the blood to Cesalpinus rather than to Harvey. The author's literature comes down to about 1905; hence the work of Barcroft and of Haldane, in opening up the subject of alveolar air and respiratory regulation, and the newer studies on the chemistry of the blood, do not come under discussion.

The second volume deals with internal secretion, digestion, excretion and the skin. The author is of the opinion, based largely on experiments conducted in his own laboratory in Rome, that the function of the thyro-parathyroid system is to neutralize a *materia peccans;* that in the absence of the glands auto-intoxication results, and that there is no evidence of a true internal secretion. The pituitary gland is, by implication, associated in its function with the same system, while the suprarenals, as is universally accepted, discharge into the blood-stream a substance essential to the normal metabolic processes. In the section on digestion Luciani definitely opposes the hormone theory of Bayliss and Starling, particularly in regard to the formation of pancreatic *secretin.* The literature in this volume, as in the first, is brought down to about 1905, with the result that the recent work again fails of treatment.

The third volume deals with the muscular and nervous systems. This volume appeals to the reviewer as the most attractive of the three. It is profusely illustrated and, what is perhaps of more moment, the treatment of the subject matter covers the literature to a recent date, although it is to be noted that the theories of the English school on the chemical processes in muscular contraction are not mentioned in the text. The translation follows the 1913 Italian edition and has, therefore, been made available to English readers with commendable promptness.

In conclusion, it is of interest to state that one or other of the earlier editions has been translated into French, German and Russian, a reliable indication that the work has been widely recognized as possessing true merit. D. R. H.

Exercise in Education and Medicine. By R. Tait McKenzie, B. A., M. D. Price $4.00. (*Philadelphia: W. B. Saunders Company, 1915.*)

This new edition is bound to have as great success as its predecessor. Indeed, one has only to look through it to realize the immense amount of good, available material there is in the book, not only as regards exercise in health and in education, but also in medicine. The first part of the book is devoted to exercises in general with their classifications, and contains excellent descriptions of the different systems that are in vogue throughout the world. Exercise, as it should be carried out in colleges and universities, as well as in schools and playgrounds, is dealt with fully, and there is an interesting chapter on the physical education of the blind and deaf mute. As regards exercises in medicine, there are so many conditions in which they are of great value that they need not be mentioned here. Each one in turn is gone into most thoroughly in different chapters, and new chapters have been

added on respiratory gymnastics, and the treatment of visceroptosis and functional disorders of the nervous system. The plates throughout are good and add greatly to the interest of the work.

J. A. C.

Occupational Affections of the Skin. By R. PROSSER WHITE, M. D., Ed., M. R. C. S., London. Price $2.00 net. (*New York: Paul B. Hoeber, 1915.*)

There are numerous contributions to this field of dermatologic literature, but it is always gratifying to read a treatise which correlates the facts and arranges them in a handy and attractive form.

Even if the subject-matter in this volume is not as comprehensive as might be desired, it certainly has been handled well. The index is complete and well arranged, and appropriate words are properly emphasized by being printed in heavy type, so that the reader can find his way very easily. The author quotes sources of information very freely—a splendid advantage for the student or prospective writer—although there is occasionally some apparent carelessness or some typographical error in the spelling of an author's name; for instance, Brock for Brocq, Kienboch for Kienböck.

A book of this type is always a welcome addition to the literature of diseases of the skin. It emphasizes particularly the fact that many of the diseases met with in practice have a definite cause. It should naturally be the object of every physician who is called upon to treat a disease of the skin to inquire minutely into any probable cause; and this cannot be done too painstakingly; for, after all, this must in great part be the basis or rationale for an intelligent therapy. Moreover, if one could add to this a knowledge of the pathologic process involved, the way to therapy would be very clear. A great many practitioners have yet to learn the lesson that in dealing with diseases of the skin prophylactic and palliative measures are factors in therapy upon which too much stress can hardly be laid.

A perusal of this little book almost naturally recalls these thoughts to one's mind. The volume should, therefore, claim a place on the shelves of all physicians as a genuine book of reference for many conditions of the skin, which at first might appear to baffle any attempts at treatment.

I. R. P.

Medical Lectures and Clinical Aphorisms. By SAMUEL JONES GEE, M. D. Cloth, $2.00. (*New York: Oxford University Press, 1916.*)

This little volume of Dr. Samuel Gee will give the reader a great deal of pleasure. It is so full of ideas and shows most clearly Dr. Gee's splendid grasp of clinical medicine. The account of the conflict of the medical profession with smallpox forms a most interesting chapter.

His aphorisms are to the point in most instances and remind one very much of some of the sayings of the ancients, written many centuries ago, but with such revision as brings them up to date.

J. A. C.

The Backwash of War. By ELLEN N. LA MOTTE. Cloth, $1.00. (*New York and London: G. P. Putnam's Sons, 1916.*)

This series of war sketches reveals much keenness of insight and a genuine literary gift, by which the wards of the army hospital and the daily life of the sick and wounded are pictured with unmistakable vividness and reality. We see, as with our own eyes, the dirty, disordered wards, the distressed patients, the insufficient heating and lighting and the lack of comforts, which no amount of good nursing can remedy. Some of the sketches are touching and pathetic in the extreme; others portray human nature at its worst—a sordid Belgian mother who reluctantly remains to see her son die, two or more physicians of loose morality, a priest "with a yellow beard" seeking forbidden fruit, drunken orderlies and the like. The general effect of the little book is to make one pessimistic and unhappy. It is a depressing contrast to the little sketch, "A Joy Ride,' by the same writer in a recent number of the *Atlantic Monthly*. One is tempted to ask, *Cui bono?* Human nature has its high and low aspects. We are stimulated to attain higher levels by deeds of heroism and self-sacrifice; tales of brutalities and gross happenings, on the contrary, depress and lower the standards of thought and effort. Why stir up "the dirty sediment at the bottom of most souls"?

H. M. H.

Practical Physiological Chemistry. By PHILIP B. HAWK, M. S., PH. D., Professor of Physiological Chemistry and Toxicology in the Jefferson Medical College of Philadelphia. Fifth edition. Revised and enlarged. Cloth, $2.50. (*Philadelphia: P. Blakiston's Son & Co., 1916.*)

The new edition is distinctly different from the earlier ones; the book has been enlarged, new chapters appearing on nucleic acids, gastric analysis, intestinal digestion, blood analysis and metabolism. Its character has also changed. Whereas formerly it was essentially a book for medical students and practising physicians, its scope has now been broadened so that it will be of considerable value to the clinical laboratory and research workers.

In tending, however, to become a compilation of the most satisfactory procedures and methods of analysis in physiological chemistry, the work has lost some of the author's style and taken on much of the character of an encyclopedia of methods. The more important methods have been emphasized by the author in heavy type. The book should prove very useful to all medical men.

H. L. H.

The Physiology of the Amino Acids. By FRANK P. UNDERHILL, PH. D., Professor of Pathological Chemistry, Yale University. Cloth, $1.35. (*New Haven: Yale University Press, 1916.*)

At present there is no book or monograph which furnishes an adequate and up-to-date summary of the part played by amino acids in the physiological processes in the human organism. This has been a distinct detriment to those engaged in the practice of medicine, as well as to the scientist interested in problems of metabolism and nutrition. The literature on this subject contains so many difficult details and covers so many pages that it is an extremely arduous task for anyone to devote sufficient time and energy to cover it with any degree of thoroughness. Frank P. Underhill, Professor of Pathological Chemistry of Yale University, has attempted to supply this need in the present volume. In the preface he states: "It has been, therefore, the aim of the writer to gather in one place the results which have thus far been obtained in the field of the biochemistry of the amino acids, thus affording the busy practitioner and others, whose resources for consulting original communications are limited, an opportunity of gaining a knowledge of the present-day problem in this field of nutrition." In order to fulfill his task, the author describes in a concise and clear way the origin of amino acids from proteins, the metabolism of amino acids and proteins and the rôle which amino acids play in health and disease, as in growth, intestinal putrefaction, etc. The book, as stated, is supposed to be for the general practitioner. In consequence the discussion of the subject is not complete and references to the literature are not exhaustive. From the clinician's point of view the book is an admirable one for those who desire a résumé of the subject from the strictly physiological chemical side. The clinical application of chemistry of the amino acids, such as the D:N ratio in diabetes mellitus, intestinal putrefaction, acidosis, etc., has not been given its proper value. It is to be hoped that from this book there may eventually result two volumes of which science

and clinical medicine are much in need: first, a thorough study of the whole subject of protein metabolism with a complete bibliography; second, a volume such as the present one with the addition of an adequate discussion of the practical clinical application of these problems. H. O. M.

A Laboratory Course in Serum Study. (Bacteriology, 208.) By Hans Zinsser, J. G. Hopkins and Reuben Ottenberg. (*New York: The Macmillan Company, 1916.*)

This little book, being a protocol of a laboratory course in serology given by the authors at the College of Physicians and Surgeons, Columbia University, New York, is not presented as a manual of technical methods or as a text-book of serology, but "describes only work actually done with the students." In most instances only one method of procedure is detailed, as, for instance, on page 18 where the technique for obtaining blood from the carotid artery of a guinea-pig is outlined, no mention being made of the convenient cardio-puncture which accomplishes the same results. In spite of this, however, by reason of the minute instructions in approved methods, it should be found useful by many who, without previous training in routine technique, wish to undertake the commoner forms of serological diagnosis. Preeminently the book will find its field of usefulness in the class-room, both to student and teacher; to the student because of its clearness and practicability, and to the teacher because of the detailed way in which the course is outlined throughout and adapted to the conditions of the class-room.

The course as outlined is calculated not only to teach the elements of serology in an attractive way, but also to train students in experimental methods. As such it is to be highly commended. The authors have made practical use of a demonstration in immunity by including as part of the course the immunization of the students against typhoid.

On the whole this book maintains the standard of excellence the profession has learned to expect from this laboratory.

F. A. E.

Practical Points in the Diagnosis and Treatment of Heart Disease. By E. M. Brockbank, M. D. Second edition. Cloth, $1.25. (*New York: Paul B. Hoeber, 1916.*)

With the exception of the parts dealing with the heart sounds and murmurs, clearness has been sacrificed to brevity.

There is no mention of lues in relation to lesions of the aortic valve nor of the removal of focal infections under treatment. There is also no mention of the associated physical signs to help in the differentiation of the murmurs. The book is well bound and well printed. D. W. C., Jr.

The Art of Anæsthesia. By Paluel J. Flagg, M. D. Cloth, $3.50. (*Philadelphia: J. B. Lippincott Company, 1916.*)

The book contains much practical matter which should prove of interest to the student of anæsthesia. It sets forth in a simple and expressive form the essential laws of anæsthesia drawn from the wide personal experience of the author. In its clearness and simplicity it is most convincing. If Dr. Flagg's teachings were taken to heart by beginners in the art, the effect for good would surely be felt.

Burdett's Hospitals and Charities, 1916. Being the Year Book of Philanthropy and the Hospital Annual. Containing a review of the position and requirements, revenue and cost of the charities. An exhaustive record of hospital work for the year, etc. Twenty-seventh year. By Sir Henry Burdett, K. C. B., K. C. V. O. Author of "Hospitals and Asylums of the World," etc. (*London: The Scientific Press, Limited.*)

As will be seen by the title, Burdett's review for 1916 has now reached its twenty-seventh year. The appearance of the present volume has been much delayed by hindrances incident to the war, such as the difficulty in securing data for the reports and the increased cost of production consequent upon the scarcity of labor and the higher price of paper. The usual carefully analyzed statistics are given, but it is noticeable that the hospitals themselves have not cooperated to the same extent as formerly. The statistics are for the year 1914.

The author tells in glowing terms of the marvelous effect of the great war upon voluntary hospitals and also upon the methods of individual workers, and of the great improvement which has come about in the administration of hospitals, by which they have been changed from civil to military organizations. He also speaks of the improved morale of the hospitals as the result of the extraordinary cheerfulness, endurance and patience shown by soldier patients, who seem to have been grateful and appreciative for all done for them. It is interesting to note that the presence of these soldiers has produced increased revenues because of personal appeals for aid. There have been many changes in the staffs of the hospitals by reason of the fact that physicians have gone to the front to take care of sick and wounded soldiers. There has been a great increase in the number of hospital beds. It seems almost incredible that this increase should have amounted to 100,000 beds.

We regret to see that the editor feels that his excellent and useful work has not been duly appreciated in England because the thorough discussions of general hospital matters have not produced abundant fruit in increasing legacies to the hospitals. He also feels keenly the fact that the book has not been properly noticed by the newspapers. It would seem, however, that while the book may not make a popular appeal or furnish such material as newspapers desire for startling and sensational head-lines, it none the less has a fixed place in the public mind as a careful, painstaking and authoritative review of all which pertains to hospital work year by year.

The present volume speaks of post-graduate medical teaching, of training school facilities in poor-law infirmaries, and contains a list of territorial hospitals. The chapters are interesting but brief.

We regret to see an intimation on the part of the accomplished editor that he anticipates relinquishing his editorial work. He laments that the position which he is to vacate when he arrives at the age of three score years and ten has not yet been filled. It is to be hoped that the same guiding hand that has presided over the book during the past 27 years may still look after it for an indefinite future. H. M. H.

The Treatment of Diabetes Mellitus, with Observations upon the Disease, Based upon 1000 Cases. By Elliott P. Joslin, M. D., Assistant Professor of Medicine, Harvard Medical School, etc. Cloth, $4.50. (*Philadelphia: Lea & Febiger, 1916.*)

Recent improvements in the treatment of diabetes—mainly through the introduction of fasting and the emphasis on the value of physical exercise by Dr. Allen—have created a demand and need for an up-to-date text-book on the treatment of diabetes. A wide and successful experience in treating diabetes, a keen appreciation of the value of physiology and laboratory methods in this disease, and an admirable ability to systematize, combine to make Dr. Joslin an almost ideal author for such a book.

Section I of the book begins with the author's distinct definition of diabetes mellitus, and consists in the main of statistics, gathered largely from his own cases. Especially interesting is the résumé of the factor of heredity and the unique method of discussing the etiology of diabetes. Section II treats of the pathological physiology of the diabetic, including a long discussion of acidosis. Section III is entitled "The Examination of the Urine, Blood and Respiration," and consists largely of descriptions of well-chosen methods. Section IV contains a discussion of the

dietetics of the diabetic—the energy, carbohydrate, fat and protein requirements and the availability of various foods for meeting these needs. Section V takes up the treatment; one finds here the simple scheme which he had previously published, augmented by the description of cases illustrating the "sources of danger." The problems of impending coma, of surgery, of pregnancy in diabetes are fully discussed. The author is a firm believer in educating his patient; thus, in Section VI, there is a "primer" on "What every diabetic should know." Other helpful points in the practical management of cases, as sample diets, charts and food tables, are included in the last two sections.

Very few faults can be found in the book; possibly the tables on food values might better have been less scattered; the frontispiece seems rather unfortunately overemphasized. But the virtues of the book completely hide its faults. It is admirably written, the explanations are simple and well presented. The book should claim a prominent place in the library of every practitioner.

H. L. H.

Diseases of the Skin. By RICHARD L. SUTTON, Professor of Diseases of the Skin, University of Kansas School of Medicine. (*St. Louis: C. V. Mosby Company, 1916.*)

A book by one who has had such a wide experience in dermatological fields as Dr. Sutton and who has been such a constant contributor to dermatological literature cannot fail to arouse considerable interest when it first appears for public inspection.

The text has 916 pages, with 693 illustrations and 8 colored plates. It presents in a conservative manner such new lines of treatment as the "autogenous serum injections," and incorporates recent investigations such as Rosenow's work on Herpes Zoster and that of Clough on foot and mouth disease in man.

The author is to be especially congratulated on the large number of excellent photographs that illustrate the book. The various types and modifications of most of the diseases of the skin are well represented in a carefully selected series. The pathology is fully discussed, and there are a number of very good microphotographs.

Somewhat iconoclastic ideas are advanced in the discussion of eczema, the refuge of the general practitioner and often of the specialist, when it is referred to as "a sort of dermatological scrap-heap"; however, most of us must acknowledge that our conception of this disease is often very diffuse and indefinite.

Dr. Sutton's book, on the whole, is clear, the subjects being presented in an easily digested form. It is up to date, but not loaded down with a lot of obsolete literature, and the illustrations are numerous and excellent. It can be highly recommended to anyone seeking dermatological knowledge, whether it be the student hunting fundamental facts or the specialist attempting to place some of the rare skin manifestations.

L. W. K.

Surgical and Gynecological Nursing. By EDWARD MASON PARKER, M. D., F. A. C. S., and SCOTT DUDLEY BRECKENRIDGE, M. D., F. A. C. S. 134 illustrations. Cloth, $2.50 (*Philadelphia and London: J. B. Lippincott Company, 1916.*)

This work is a worthy contribution to the many small volumes published for the use of nurses. Its contents are limited to the care of surgical and gynecological patients, and it contains sensible material and practical suggestions for the care of these cases. The chapters dealing with the comfort of the patient and post-operative complications are valuable, and the descriptions of the various methods of bandaging are complete. Fewer pictures of the sterilizers would have sufficed and the space might have been utilized for illustrations of methods for giving treatments, such as bladder catheterization and irrigation, vaginal douches and the proper care of the infusion apparatus and the breast area during hypodermoclysis.

Medical students in the last two years of the course can also read the book with profit.

C. W. V.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles on Treatment, Medicine, Surgery, Neurology, Pædiatrics, Obstetrics, Gynecology, Orthopædics, Pathology, Dermatology, Ophthalmology, Otology, Rhinology, Laryngology, Hygiene, and other Topics of Interest to Students and Practitioners. By leading members of the medical profession throughout the world. Edited by H. R. M. LANDIS, M. D., Philadelphia, with the collaboration of ten additional editors. Vols. 1 and 2, 26th series, 1916. (*Philadelphia and London: J. P. Lippincott Company.*)

As might have been expected from those that have gone before, these two volumes contain many excellent articles, although of unequal scope and varying importance. Among the more important may be mentioned Friedenwald's "Early Diagnosis of Gastric Cancer"; Young's "Tetanus: Lessons Gleaned from the War, Modern Research and Private Practice"; Robinson's "Auricular Fibrillation: The Cause and Its Relation to Ventricular Activity"; Bowers' "The Relation of Mental Defect to Crime"; Martin's "Colon Resection and Its Indications," and Osgood's "Orthopædic Problems Presented by the European War." It is much to be regretted that space will not permit more than an enumeration of the titles of these papers. The volumes are worthy of thorough study.

H. M. H.

Christianity and Sex Problems. By HUGH NORTHCOTE, M. D. Second edition. Revised and enlarged. Cloth, $3.00. (*Philadelphia: F. A. Davis Company, 1916.*)

This work is modestly stated by the author to be written with the expectation that after a few years it might be found to be "quietly useful." It is written as a study of a difficult subject and not as a polemic, to advance a theory or to support a cause. It contains a careful statement of the problems of sex and gives the teachings of the Bible and of the teachers of the church bearing upon them. There seems a little tendency to rely too much upon authority and too little upon reason in the final settlement of some of the problems. The complexity of the problems involved forbids any critical consideration of them in the present review. The fair-mindedness and sincerity of the author win confidence. The book is in marked contrast to the usual treatises upon sex matters, and can be commended to the careful reading of all persons who are honestly in search of guidance.

H. M. H.

Sexual Impotence. By VICTOR G. VICKE, M. D., Consulting Surgeon to Mount Zion Hospital, San Francisco. Fifth edition. Enlarged. Cloth, $2.25. (*Philadelphia and London: W. B. Saunders Company, 1915.*)

The appearance of a new edition of this work after a period of three years indicates a steady demand for the book. The additions to the last edition are largely in the direction of treatment. The author has very sensible ideas upon psychotherapy and is much encouraged by his experience with psychoanalysis. The whole book is judicious and characterized by moderation and good common sense.

H. M. H.

Clinical Disorders of the Heart Beat. By THOMAS LEWIS. Third edition. Cloth, $2.00. (*New York City: Paul B. Hoeber, 1916.*)

That the second edition of Dr. Lewis' book should have been exhausted in two years speaks for its popularity with the medical profession. The subject-matter is presented in the same order as in the former edition. Minor changes have been made in words here and there throughout the text. In the chapter on heart block reference is made to adrenalin in the treatment of the "fit," but the author merely states that it has been suggested. In the treatment of the "Abrupt onset of partial heart block"

full exposure to the open air, the author thinks, "deserves a thorough trial."

The insertion in the chapter on auricular fibrillation of the influence of this condition on thrombosis and infarction is an addition to the work.

More extended observation seems to have shown the greater frequency of "alternation of the heart" in general hospital patients than was given in the last edition.

Throughout the present work the illustrations and figures of the former edition have been retained with their explanations.

The book presents the subject clearly and concisely and is too well known to require a more extended review.

H. R. C., Jr.

The Treatment of Acute Infectious Diseases. By Frank Sherman Meara, M. D., Ph. D., Professor of Therapeutics in the Cornell University Medical College in New York City. (*New York: The Macmillan Company, 1916.*)

The purpose of this volume on "Treatment of Acute Infectious Diseases" is to present its material in a thoroughly practical and useful way. The author discusses the therapy of the acute infections in a fascinating manner. He drives home his ideas in ringing sentences that leave no doubt in the reader's mind as to his exact meaning. Such episodes in the thread of thought as the following are not uncommon: "The contrast between a well-ordered, neat, cool sick-room, and a hot, stuffy room, with six or ten visitors, gas jets in full action and babel and chaos regnant, is one of the most striking that can be witnessed." Experimental and scientific observations are quoted as far as possible to furnish a reasonable basis for each therapeutic procedure. Of course, however, many of these still rest on clinical empiricism, and it is in this connection that Professor Meara's wide experience and his keen judgment give the constant use of the personal pronoun, "I am convinced" and "I believe," a significance that cannot be underestimated. The presentation of the subject is complete, thorough and very lucid. By means of subheadings attention is called to bed, room, diet, drugs, specific treatment, etc., in each disease. Furthermore, there is a very well-arranged and suggestive summary at the end of each chapter. The book is complete to the minutest detail in its therapeutic directions; it is written in a very lucid style, so that the subject-matter can be quickly assimilated without any doubt on the reader's part of the author's meaning, and finally, the judgment exhibited in the principles of treatment advocated is excellent. H. O. M.

Gynecology. By William P. Graves, M. D., F. A. C. S., Professor of Gynecology at Harvard Medical School. 8°. 770 pp. 424 original illustrations; 66 in colors. Cloth, $7.00 net; half morocco, $8.50 net. (*Philadelphia and London: W. B. Saunders Company, 1916.*)

New ideas and an attractive arrangement of the material characterize this recent addition to the works on gynecology. The subject is divided into three parts, dealing respectively with the physiology and relationship of gynecology to the general organism, gynecological diseases and operative gynecology. One important contribution, thoroughly treated in the first section, and mentioned throughout the volume in connection with various conditions, is the consideration of the glands of internal secretion. This field of medicine now being extensively studied, and heretofore omitted from works on gynecology, is dealt with in a practical way; and this portion adds much to the completeness of the work.

A full list of the gynecological diseases is included in the second part and the descriptions here given, although in many instances brief, are accurate and clearly set forth. In the operative section the usual gynecological operations are described, and many are accompanied with illustrations, more or less diagrammatic. In a work of this size one would expect more consideration to be given to the pathological conditions of the urinary system and their treatment, and this lack materially detracts from the book's sphere of usefulness. Extra-uterine pregnancy and dysmenorrhea are well treated, but no mention is made of the subject of threatened or incomplete abortion.

The volume is fully illustrated with microscopic drawings and illustrations. The latter, which are by the author, are creditable productions and readily convey the idea intended. Those on pages 522 and 523, however, are misleading and should be improved.

In brief, the work is well written; it contains the important parts of gynecology concisely stated and attractively presented. It will be of decided value to both students and practitioners.

C. W. V.

Home Care of Consumptives. By Roy L. French. 12°. 200 pp. Cloth, $1.00. (*New York: G. P. Putnam's Sons, 1916.*)

The author is a social worker who has been actively identified with tuberculosis work for several years and has even had the disease in his own family.

For patients discharged from sanitaria the book reiterates principles laid down in the institution and emphasizes the need for lifelong care and watchfulness. For patients without the advantage of sanitarium instruction it deals in a definite, practical way with questions of home nursing without expensive equipment, with the social aspects of the disease and the relation of patient to physician. Without unwarranted optimism it offers substantial encouragement to the patient and his family. Dispensary physicians will find in it many useful suggestions.

M. A. H.

Nerves. By David Fraser Harris. University Library of Modern Knowledge. (*New York: Henry Holt & Co., 1916.*)

This little octavo volume contains 10 chapters together with a glossary, useful for the layman or student, and an index. In his preface the author says: "The following pages . . . . attempt to explain in non-technical language the place and powers of the nervous system." And later: "It is hoped that those whose previous knowledge of physiology and psychology is small may learn something of the way in which this complicated system does its work; and that those who happen to know something of these subjects may yet gain more from an account of innervation which is as accurate as popular terminology allows it to be." The book is at once readable and instructive, and anyone of either category of readers who takes it up will read it through. At all times, science tempered by sound common sense can hardly fail to be attractive; and this book contains both. F. R. S.

Gould's Practitioner's Medical Dictionary. Third edition. Revised and edited by R. J. E. Scott, M. A., B. C. L., M. D., of New York. XX + 962 pages. Flexible cloth, round corners, marbled edges, $2.75. (*Philadelphia: P. Blakiston's Son & Co., 1916.*)

The compactness, clearness of type and convenient form of this admirable dictionary commend it to every general practitioner. It includes all current words and terms and gives concise and clear definitions with the correct pronunciation of each. In the present edition 20,000 new words have been added, and the volume of about 1000 pages contains upwards of 70,000 words in the aggregate. It is worthy of high praise. H. M. H.

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